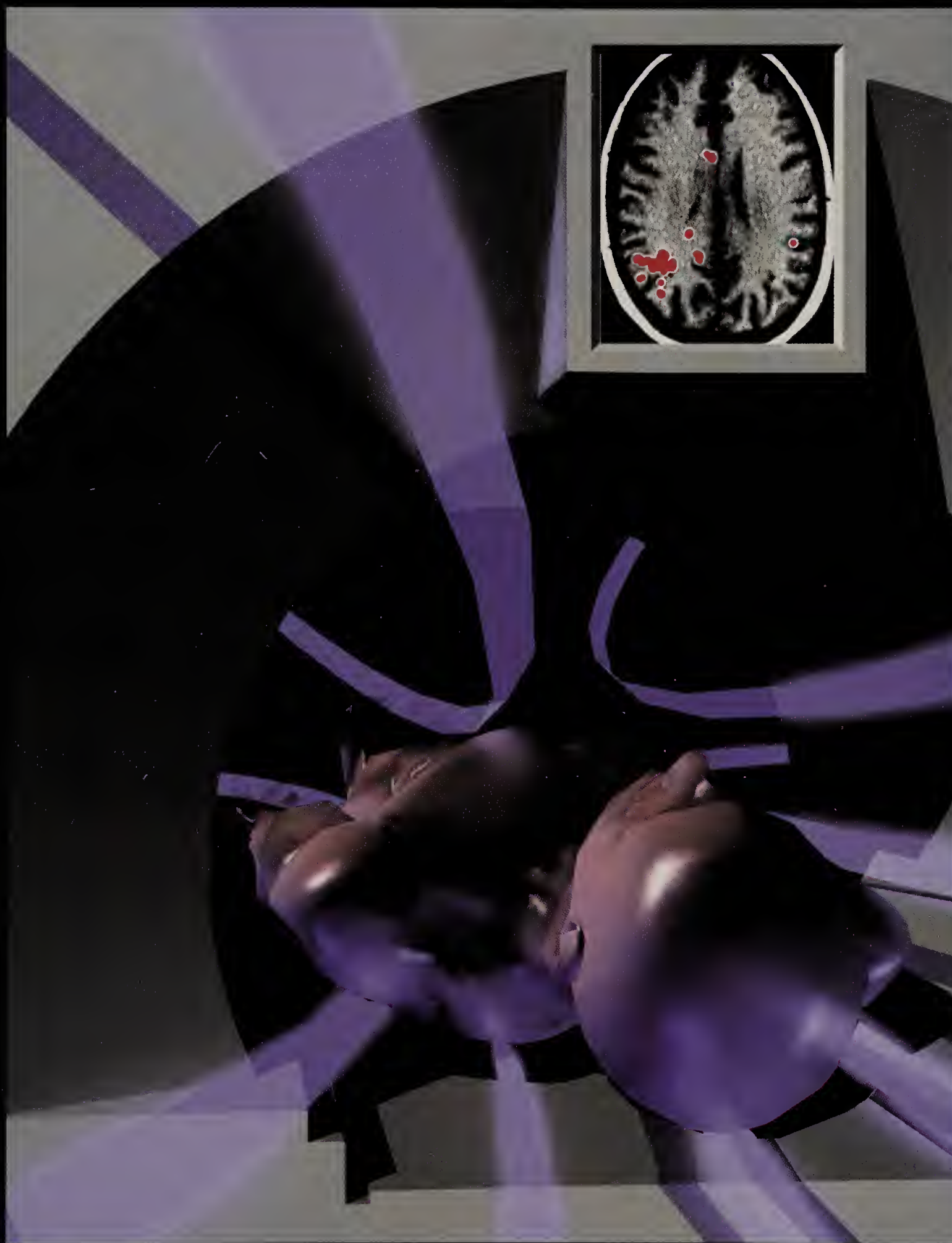


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Medical Journal



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Editorial

It is with great pleasure and excitement that we present the first edition of the seventy-fourth volume of the University Toronto Medical Journal. The UTMJ is completely organized and written by the students of the Faculty of Medicine at the University of Toronto. We would like to thank all the students who contributed articles, assisted with editing, or produced artwork. The UTMJ has enjoyed a long and illustrious history, highlighting the works of many of the great clinicians, scientists, and medical students that make up the University of Toronto Faculty of Medicine community. Our circulation is over one thousand and the UTMJ continues to reach physicians around the world. We hope to carry on this tradition with the upcoming edition, while adding new features that we believe will make the Journal more enjoyable to our readership.

This volume of the Journal will continue to feature articles on a number of topics with relevance to current medicine. Although readers will find submissions covering the traditional biomedical disciplines, we hope to also to feature articles on broader fields such as medical ethics, international health, and community medicine, all of which are becoming increasingly important in today's practice of medicine. This current issue features five articles covering a spectrum of medical topics. Our feature submission is a review of functional MRI. This is a new method of imaging the physiology of the central nervous system and is beginning to replace the technique of PET scanning in providing insights into physiological and pathological patterns of brain activation. The reader will also find a fascinating review of prostate cancer and its diagnosis. This is an important topic for all medical students and primary care providers who need to be aware of the high prevalence of this disease and the controversies involved in screening for it. From the field of endocrinology, we present a paper on the diagnosis and management of Graves' disease. We hope that this article will provide a useful approach to this interesting immune-mediated condition. From pathology, we offer a case report of pneumococcal aortitis. Although this disease is rare, it can have devastating consequences for the patient if left undiagnosed and untreated. Finally, we are pleased to present a paper dealing with ethical issues faced by clinical clerks during their training. This paper highlights the growing importance for ethical training in medical education, while presenting some interesting ethical issues that clinical clerks may face.

We are pleased to feature a new section to the UTMJ, Case Records of the University of Toronto Medical School. Modeled after a similar section in the *New England Journal of Medicine*, this section is a clinicopathological correlation exercise that provides the reader with an approach to a difficult diagnostic problem. In this issue, we feature a case of a man who initially presented with flank pain, was worked up, sent home, and suddenly died ten days later. It is a fascinating case that we are sure will test both medical students and physicians. We are deeply indebted to our clinician discussant, Dr. Allan Detsky for volunteering his time and clinical acumen to this case and to Michael Pollanen Ph.D. (9T9) for providing the case and the pathological discussion.

Our News and Views section will continue to provide readers with some of the latest developments as well as provide a forum for readers to express their opinions on any pertinent topic. In this issue, the reader will find a broad selection of pieces detailing developments in and around the University of Toronto community. We encourage readers to submit letters with views on any of the Journal's contents or any other topic of interest.

The Book Reviews section and Quick Diagnosis section are both returning for the seventy-fourth volume. In Quick Diagnosis we present some common histopathology of the kidney to challenge our readers.

Our final new initiatives in the seventy-fourth volume reflect the growing importance of computers and information technology as medicine moves into the next century. As such, we have created a World Wide Web site to present the UTMJ on the Internet. This site is introduced in our News and Views section. In addition, as our final new section, we present a series of computer software reviews. As a special introduction to this section, our first issue features a discussion of two new programs designed to aid physicians and students in the differential diagnosis of disease. With the assistance of Dr. Peter Webster, a discussion ensues of how far computers have come and how far they still have to go to aid physicians and students.

Finally, we would like to acknowledge our faculty advisor, Dr. Andrew Baines for providing direction and support. As always, we thank our patrons and subscribers, who recognize the importance of the UTMJ as a vehicle for medical students to publish their accomplishments. Without the help of our patrons and subscribers, the Journal would cease to exist.

We hope that all readers enjoy this issue and we look forward to providing further issues throughout the year and maintaining the quality that UTMJ readers have come to expect.

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Methadone Treatment in Toronto

Raquel Adelstein, M.Sc.
(9T8)

In May of this year, the Addiction Research Foundation (ARF), in keeping with its Harm Reduction policy, announced a number of changes to its methadone treatment program with the goal of making the program more user-friendly. Changes included decreased emphasis on testing to monitor illicit drug use, increased access to "carries" (take-home methadone for client use) and replacement of mandatory counseling with optional, client-centered counseling. With less emphasis on drug testing, the program acknowledges that total abstinence may not be a realistic goal for all clients. Rather, maintenance in methadone treatment, with an attendant reduction in IV drug use and associated harm, is seen as a realistic goal with the aim of lowering overall risk and the spread of such diseases as HIV, TB and Hepatitis B and C. Expanded access to "carries" allows clients to commit to full-time jobs and thus to develop a more stable lifestyle.

While no additional funding is slated for ARF's new methadone program, the restructuring will permit accommodation of 260 clients, an almost three-fold increase from its previous capacity of 100 people. As always, HIV

Bisphosphonates: New(ish) Drugs for an Old Disease

Michelle Farrugia, M.Sc. (9T8)

Osteoporosis has a huge impact on the health and well-being of post-menopausal women. Fractures result from decreased bone mass and altered micro-architecture of bone, most commonly in the vertebrae. These crush fractures lead to pain, kyphosis and reduced height. Also common are hip fractures, which are associated with the greatest morbidity and mortality of all fractures in this population (the one year mortality rate from a hip fracture and subsequent complications is 20%).

While prevention of osteoporosis and resultant fractures through exercise, dietary calcium, and fall prevention is critical, impeding bone loss with the aid of medications is assuming increasing importance in managing the osteoporotic patient. For post-menopausal women, the best choice is estrogen replacement therapy (ERT) initiated at menopause. ERT prevents bone loss and reduces the risk of fracture if taken long-term. It also confers cardioprotective benefits. Yet many women choose not to take it for reasons such as increased risk of breast or endometrial cancer. For these women, a number of other agents can be used to minimize bone loss, including calcium supplementation, subcutaneous calcitonin, fluoride, and most recently, bisphosphonates.

In osteoporosis, bone loss results when bone resorption exceeds bone formation. While the mode of action of bisphosphonates is not entirely clear, their most important function is to inhibit bone resorption. Two bisphosphonates, etidronate and alendronate, have recently been approved for use in treating, although not preventing, post-menopausal osteoporosis in Canada.

Etidronate is not a new drug; it was originally developed as a washing powder and is now produced by the pharmaceutical division of Procter & Gamble, a company which manufactures more than a few soap products. The ability of etidronate to inhibit bone resorption was noted in the 1960's and since then it has been used as a treatment for Paget's disease of the bone, which is characterized by increased osteoclast activity and excessive bone resorption. The use of etidronate in post-menopausal osteoporosis is more recent. Because of concerns that etidronate might cause abnormal bone mineralization, it is used cyclically when treating osteoporosis: 400 mg for 14 days out of 90, with calcium taken daily during the rest of the cycle. For a few years in the early nineties, a limbo existed in which some physicians prescribed etidronate for their osteoporotic patients even though it had not been officially approved for this use. Then, some multi-center, randomized, double-blind, placebo-controlled clinical trials showed increases in hip bone and vertebral density as well as reductions in vertebral fractures in etidronate-treated patients, and this led to the recent approval and marketing of the drug for use in osteoporosis.

Unfortunately, one study showed more non-vertebral fractures in etidronate-treated patients than in placebo-treated patients. However, this was rumoured to be due to the fact that many of these women felt so good while taking etidronate that they started painting houses, going on safari and engaging in other such adventurous, high risk behaviours. Accordingly, traumatic fractures in sites not associated with osteoporosis or aging were excluded and the data then showed no difference in fracture occurrence between etidronate and placebo-treated groups (except vertebrae). While previously marketed under the name Didronel, etidronate for osteoporosis is now marketed under the name Didrocal. It comes in a box with 14 tablets of etidronate and 76 tablets of calcium (500 mg) in blister packs, for \$55 (plus dispensing fee), and is approved by the Ontario Drug Benefit Plan (ODB). Didronel is still available, and costs \$20 (plus dispensing fee) for a 14 day supply. Since a large bottle of calcium supplements or antacids will provide the required calcium for the remaining 76 days for much less than \$35, the cost of Didrocal does seem to be somewhat inflated.

The newest bisphosphonate on the market in Canada is alendronate. Because it is about 1000 times more potent than etidronate, it can be used at doses which do not inhibit bone mineralization, and can thus be taken daily (10 mg). A multi-center, randomized, double-blind, placebo controlled clinical trial demonstrated that alendronate-treated women had increased bone mineral density at all skeletal sites compared to women receiving placebo. There was also a 48% reduction in vertebral fractures, although the incidence of non-vertebral fractures was not significantly different between the two groups. Alendronate is marketed by Merck Frost as Fosamax. A 90 day supply costs \$180 (plus dispensing fee) but is not yet covered by the ODB.

A few more bisphosphonates are currently in clinical trials - you may soon see risidronate, tiludronate, clodronate and pamidronate at a pharmacy near you. Although bisphosphonates seem promising, questions remain. It is not known if these drugs will be useful in other populations affected by osteoporosis such as elderly men, corticosteroid users, and chronic bowel, kidney, and renal disease patients. It is not known if they will actually prevent osteoporosis before it starts. And finally, the effect of bisphosphonates on hip fractures remains unclear. In all the studies mentioned, the incidence of hip fractures was too low to draw conclusions. Since these are one of the greatest contributors to morbidity, mortality, and health care costs in osteoporotic patients, this is perhaps the most relevant question. Only when it is answered will the benefits of bisphosphonates in the treatment of osteoporosis be fully understood.

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positive or pregnant clients will have immediate access to the program.

In order to increase access to methadone treatment, ARF is working to increase the number of treatment providers in Ontario by offering training to interested students and community physicians. Through collaboration with the Ontario College of Physicians and Surgeons, ARF hopes to relax guidelines for the licensing of practitioners interested in incorporating methadone treatment into their practices and to establish links between community practitioners and experts in addiction medicine.

Advances in Hormone Replacement Therapy

Karen Gronau, M.Sc. (9T8)

It is well known that heart disease risk is decreased in postmenopausal women by taking estrogen. However, because of the high rate of endometrial hyperplasia induced by unopposed estrogen, this regimen is not acceptable for use in women with uteruses. Combined estrogen/progestin therapy has been recommended for this group and recent studies have shown that cardioprotective benefits are similar to when estrogen is taken alone. The exact mechanism by which estrogen exerts its cardiovascular effects remains a mystery. Various factors such as changes in lipid and carbohydrate metabolism, blood pres-

sure, coagulation factors, and endothelial function have been suggested. Among these, evidence indicates the crucial effect may be on lipoproteins, with reduction of low-density lipoproteins (LDL-C) and growth of the high-density lipoprotein (HDL-C) fraction.

Thus, recent findings that women taking unopposed estrogen had greater increases in HDL-C than women taking estrogen/progestin indicate that current hormone replacement therapy (HRT) regimens are not optimizing cardioprotection.

To assess the cardiovascular effects of various HRT protocols, a three year, multicentre, randomized, double-blind clinical trial was performed in the United States, and the results were published in JAMA last year. The purpose of the trial was to determine the effects of different HRT regimens on various cardiovascular risk factors, including HDL-C and blood pressure. The four regimens examined were: placebo, unopposed estrogen, estrogen plus medroxyprogesterone acetate (MPA, the standard progestin used for HRT) and estrogen plus cyclic microionized progesterone (MP).

All three HRT protocols were found to lower LDL-C levels and increase HDL-C levels. With respect to increasing HDL-C specifically, unopposed estrogen was the most effective treatment. However, estrogen/cyclic MP treatment decreased LDL-C and increased HDL-C more than estrogen/MPA therapy. Thus, for post-menopausal patients with intact uteri, physicians may want to consider HRT with estrogen/MP as an alternative to the current standard treatment, estrogen/MPA.

Substance Abuse Curricula in Ontario Medical Schools

Karen Gronau, M.Sc. (9T8)

Project CREATE is a program that aims to develop and implement a new curriculum on substance abuse in Ontario medical schools. The Addiction Research Foundation, the Lawson Foundation, and Max Bell are funding this initiative. The goal is to construct a multidisciplinary substance abuse curriculum that will be both more useful and more interesting for medical students than the teaching currently in place. It has been shown that medical students sometimes have negative attitudes towards alcohol and drug abusers which can become more negative as their level of training increases.¹ This bias can act as a barrier to effective diagnosis and treatment of substance-dependent patients. The relative lack of physician education in this area is in part due to the fact that until recently, alcoholism was thought to fall under moral or legal, rather than medical, jurisdiction. Now that addiction is recognized as a disease, doctors have increased responsibilities towards addicts in their practices, but many do not have appropriate training. Surveys of practicing physicians have shown that many do not feel confident of their skills in this area. It is the role of medical education to respond to this and to educate students accordingly. However, because older physicians have not been extensively trained in the field, many do not feel they can teach effectively in this area. Furthermore, some will convey their own preconceptions to their students. Thus, they may not teach students appropriate assessment and treatment skills. It is necessary for physicians to be able to recognize early, non-stereotypic alcoholics, as well as to treat the underlying disorder rather than just its complications in more advanced cases. To better educate doctors about attitudes toward and treatment of substance-addicted patients, intervention in the pre-clinical years before attitudes and practices are fixed is recommended.²

Various teaching tools have been employed at American medical schools to address this issue. At the University of Rochester Medical Center³ and the University of Washington,⁴ recovering alcoholics recruited from local Alcoholics Anonymous groups act as patient educators to third year medical students, thus giving them the opportunity to interview real patients and to practice dealing with resistance and denial.³ The University of Southern California employs a peer teaching program, in which interested students are educated about alcoholism, which they then teach to first year medical students. Issues emphasized include encouraging students to examine their own attitudes and biases towards alcoholism and to realize that these could act as barriers to providing effective treatment to alcoholics and learning how to screen for alcoholism when it presents more subtly.⁵ The workshops were modified based on student feedback and the program plans to expand to all years, emphasizing treatment of alcoholics and issues of physician impairment. At the University of Minnesota⁶ and the University of California, San Diego,⁷ chemical dependency treatment centres are used as sites for clinical learning. Students are required to elicit substance use histories from addicted patients, to attend tutorials and to join a facility-based inpatient treatment team during the clerkship. At Jefferson Medical College in Philadelphia, computer-assisted instruction

modules about addiction theory and patients at risk for substance abuse earned positive student response and motivated many students to learn more about the subject.⁸ Other methods such as requiring students to attend Alcoholics Anonymous meetings⁹ and the use of standardized patients with no personal addiction history who have been trained specifically to portray addicts¹⁰ also received positive reviews from students. Project CREATE intends to examine these and other educational initiatives in detail, in order to determine which methods might function best in the Ontario medical school curricula.

In addition to curriculum issues, a program for the prevention and management of substance use disorders among medical undergraduates and doctors is planned. This aspect of Project CREATE has been christened WHIMS (Wellness, Health and Impairment in Medical Students). Recognizing substance abuse in oneself and one's colleagues, and knowing what to do about it is an integral component of the WHIMS initiative. Why target medical students with this information? American studies of depression and substance use patterns in medical students indicate that they are a population at risk. It has been shown that approximately twelve percent of medical students suffer from depression during their first two years of medical school and one study showed that eighteen percent of a class abused alcohol.¹¹ Thus, it is essential that medical students are able to recognize the risk factors for substance abuse, both in themselves and their colleagues.

By addressing the issues of medical student education about substance abuse, student attitudes towards addicts and risk factors for recognition of impairment in oneself or one's colleagues, Project CREATE hopes to change the way future doctors deal with addiction, both in their patients and within their profession.

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Bacterial Vaginosis or Vaginal Candidiasis?

Anna Mason, B.Sc. (9T9)

Bacterial vaginosis (BV) is the most common form of vaginal infection. Various studies have found BV in 10-64% of women visiting female health clinics. If left untreated it can lead to more serious problems, such as pelvic inflammatory disease. Pregnant women with BV are at risk of premature delivery. BV is also associated with post-operative infection and endometriosis. The symptoms of BV are a foul or fishy vaginal odor, and a milk-like vaginal discharge. Diagnosis may also be made by a vaginal pH greater than 4.5 and "clue" cells (epithelial cells coated in bacteria) in the discharge. The cause of BV remains unknown. The standard treatment is metronidazole intravaginal gel, active against anaerobic bacteria.

Dr. James McGregor, professor of obstetrics and gynecology at the University of Colorado notes that, "because the symptoms of bacterial vaginosis are unpleasant, the medical community, media and women themselves have often been embarrassed to talk about the disease." It is likely that women with BV are treating themselves with over the counter medications for vaginal candidiasis or yeast infections, which has none of the possible serious complications that BV does. Thus, in addition to treating the wrong disorder, these women are putting themselves at risk of developing complications due to untreated BV.

To address this problem, doctors at a symposium held as part of the Society of Obstetricians and Gynecologists of Canada Annual Meeting urged women and health care professionals to increase their awareness and open communication on the symptoms and diagnosis of vaginal infections.

Source: Press Release FERRING

New Hepatitis A Vaccine

Anna Mason, B.Sc. (9T9)

Hepatitis A is the most prevalent type of infectious hepatitis. In Canada, epidemiologists believe that the true incidence is four to ten times higher than the 1,000 to 3,000 cases that are reported annually. The highest incidence of hepatitis A is in individuals younger than 15, who make up nearly 30 percent of reported cases. The hepatitis A virus is transmitted via the fecal-oral route and is highly contagious. The incubation period is 20 to 50 days, which allows asymptomatic infected people to spread the disease. The manifestations of hepatitis A range from subclinical to severe acute liver disease and, in some cases, death. The severity of symptoms increases significantly with age, with the most severe reactions in adults and older children. Infants often do not show any symptoms.

VAQTA™ is a new vaccine for the prevention of hepatitis A that

Laser Eye Surgery - The Straight Goods

Sohel Somani (9T8)

Have family, friends, or patients told you that they are getting tired of wearing glasses or contact lenses? Do they want to get rid of their glasses for cosmetic or work-related reasons? Is the daily hassle of cleaning contact lenses or their cost becoming a burden? If so, they have probably asked you about laser eye surgery, which is advertised extensively. While the notion of having one's vision corrected by burning the eye with a laser can be disconcerting, people are often ready for a new alternative to wearing glasses or contacts. This is particularly true for those people who are undaunted by the \$2000 per eye price tag.

Laser eye surgery is used by ophthalmologists for correction of refractive errors including myopia (near-sightedness) and astigmatism. The eye is an ideal tissue for laser use because it is an optical system and thus resembles a laser itself. One procedure among many that is done to correct refractive error is keratorefractive surgery, which involves altering the corneal surface to allow for images to focus right on the retina rather than in front of the retina (as in myopia) or to correct the curvature of the cornea as in astigmatism. Although refractive errors are not due to corneal pathology, the cornea is modified to compensate for refractive error resulting from pathology in other eye structure(s).

This concept is based on the phenomenon of corneal flattening that occurs after injury and results in a change in the refractive power of the eye, first recognized in the late 19th century. Internal surgical incisional refractive keratotomy to correct myopia was introduced in Japan in the 1940s without much success, but was later modified and improved in Russia. The Russian procedure, called radial keratotomy, involved making anterior radial corneal incisions with a surgical keratome blade, which weakened the peripheral cornea and thus led to a refractive change. In the 1980's the keratome was replaced by the excimer laser, named for the "excited dimers" of halogen gases used to generate energy photons and found to be superior to the keratome for refractive correction.

Excimer laser photorefractive keratectomy (PRK) involves direct removal of tissue in the central cornea, which then resculpts the anterior refractive surface of the eye. Once altered by PRK, this central ablation zone produces corneal flattening over the visual axis, thus reducing myopia. By changing the pattern of surface ablation astigmatism can be also be corrected. Hyperopia is corrected in a less predictable fashion by laser and thus this procedure is not routinely performed for far-sighted patients. The intended change in dioptric power is achieved by varying the depth and diameter of the ablation zone. While there is no apparent thermal damage, deeper ablations may increase the risk of subepithelial haze caused by fibroblastic keratocytes and local collagen synthesis. Patients are treated post-operatively with topical steroids and anti-inflammatory medication to inhibit normal wound healing, and this limits haze and refractive regression. Over 1 million PRK proce-

dures have been performed globally, and as of 1995, PRK has been an approved surgical procedure for the correction of myopia and astigmatism.

Despite the excellent track record of PRK, confusion over its complications has served as a deterrent to its universal acceptance amongst ophthalmologists and the public. These complications include delayed healing, less than total accuracy of refractive correction and corneal haze. Delayed healing is estimated to occur in 5-10% of patients, and is ultimately associated with little adverse outcome. Less than totally accurate refractive correction is a function of the severity of the original refractive error; outcome becomes less precise as more corneal ablation is performed. Thus, in low myopes (< -6 diopters), approximately greater than 95% achieve permanent refractive correction, while in moderate myopes (-6 d to -10 d) this success rate is lower. The correction achieved for high myopes (> -10 d) is significantly less consistent. Corneal haze occurs in about 1-2% of patients and its incidence is also linked with the severity of the initial refractive error (i.e. lower incidence in lower myopes). Fortunately, corneal haze can be managed pharmacologically as discussed above. While data for astigmatism is equally promising, a fairly common complication is undercorrection, and this will no doubt improve as new laser technology becomes more advanced.

PRK, like other forms of keratorefractive surgery, is contraindicated in patients with corneal pathology (e.g. keratoconus, keratitis), external ocular inflammation (e.g. autoimmune conditions) and refractive instability. Dr. Steve Arshinoff, an ophthalmologist who performs PRK, advises prospective patients to seek advice from an ophthalmologist experienced with the procedure. Patients should consider PRK if they desire correction of distance or astigmatic refractive error, but not for correction of far-sightedness. Also, because PRK is a surgical procedure, it is not appropriate for all people with refractive errors, although in suitable patients complications are certainly minimized. Thus, for myopes and people with astigmatism looking for an alternative to their current eyewear, laser surgery is available if the price is not prohibitive.

The University of Toronto Medical Journal and the author are indebted to Dr. Steve Arshinoff, Ophthalmologist-in-Chief, York-Finch General Hospital, for providing information for this article.

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has recently been approved for use by the Health Protection Branch of Health Canada. It is the first and only hepatitis A vaccine in Canada recommended for preventing the disease in both children and adults. Experts believe that asymptomatic children are a source in transmitting the disease to adults. By immunizing both children and adults, it may be possible to eradicate hepatitis A.

There is no treatment for hepatitis A, and the medical and economic consequences of the disease are substantial. The National Advisory Committee on Immunization has recommended that children and adults at risk of exposure be vaccinated. High-risk groups include: people traveling to countries with high or intermediate prevalence of infection; military personnel; people living in areas with high endemic rates of infection and periodical outbreaks; persons engaging in high-risk sexual activities; and users of illicit injectable drugs.

Source: Press Release Merck Frosst

Research Winner

Michael Heiber (9T8) won first place - The Sigma XI Award for Overall Excellence in Research, Poster Presentation - at the 37th Annual National Student Research Forum (NSRF) in Galveston, Texas (April 25-17, 1996). Heiber's research "Cloning and characterization of a human gene encoding a novel G protein-coupled receptor"

(supervised by Brian O'Dowd, Department of Pharmacology) was first out of 83 posters from all over the USA and Canada.

After winning the George Brown Memorial Award in the Experienced Researcher – Basic Science category at the 1996 Medical Student Research Day, January 9, 1996, Heiber was selected to attend the NSRF.

University of Toronto Medical Journal Website

Stanley Hum, B.A.Sc. (9T9)
Medical Journal Website Editor

The fall issue of each year's Medical Journal always represents a changing of the guard. A new staff starts and brings with it new ideas and added optimism. This issue is somewhat special in that respect. In addition to the paper-bound copy which you are reading, this issue marks the opening of the Medical Journal's introduction on the World Wide Web, thus propelling the journal onto the information highway and into the next millennium.

Regardless of the medium, the mission of the journal remains the same: to deliver and report on the research and views of the medical students at the University of Toronto and to inform faculty and students of current events and new developments. The journal website offers electronic access to the journal staff, feature articles of each issue and access to back issues. Its goals

Sexual Orientation Issues in Medicine

Matthew Cheung (9T9) and Renée Waterman, B.Sc. (9T9)

With the passing of Bill C-33, sexual orientation has finally been included in the Canadian Charter of Rights and Freedoms as prohibited grounds for discrimination. However, the problem of prejudice in the medical field against lesbian, gay, and bisexual (LGB) patients, physicians, and medical students remains to be resolved.

During the debate surrounding the human rights amendment, Dr. Jack Armstrong, head of the Canadian Medical Association, issued a strong statement that doctors are obligated to treat lesbians and gay men with the same respect they would give other patients.

"I want to submit fully that physicians in Canada are here to provide care to all citizens of this country, regardless of their sexual preference or orientation or for any other reasons," said Armstrong.

Despite such progress, LGB physicians, medical students, and patients are continually barraged by homophobic comments and heterosexist attitudes in the healthcare setting. According to a 1994 survey by the Gay and Lesbian Medical Association (GLMA), 51% of North American gay and lesbian medical students were verbally harassed or insulted, while 54% of students were socially ostracized due to their sexual orientation.¹ This anti-gay bias affects medical students who are "out", as well as those students who are presumed to be gay. Openly gay physicians hardly fare better, with almost one fifth of doctors reporting economic and social discrimination.² This discrimination includes refusal of medical privileges, educational opportunities or promotions, denial of referrals from other physicians, and in some cases, outright dismissal.³

Prejudice against gays, lesbians, and bisexuals in healthcare is perhaps most distressing for LGB patients. A recent report in the *Journal of the American Medical Association* reported that 63% to 89% of all doctors routinely neglect to take a sexual history.⁴ When these physicians rely on assumptions about their patient's sexual orientation, they fail to recognize that LGB patients have specific health concerns and problems. For instance, there is a greater prevalence of substance abuse in the gay community (ranging from 28% to 35%) compared to the heterosexual population (10% to 12%), and this discrepancy is thought to be due in part to the social marginalization this group experiences.⁵ Due to their frequent social isolation and low self-esteem, gay teens are more vulnerable to suicide.⁶ Other problems that might be overlooked include HIV infection, ovarian cancer, and mental health problems. Lack of knowledge about a patient's sexual orientation leads to neglect of that patient's healthcare needs. Discrimination against gays, lesbians, and bisexuals is both a health problem and a social problem.

LGB patients are not only affected by the medical profession's failure to deal with LGB issues, but are also discriminated against by physicians. In 1986, physicians belonging to a Californian medical association were surveyed about their attitudes toward gay men and lesbians. The survey found that 40% would not continue to refer patients to a gay or lesbian colleague; 40% would discourage gay men and lesbians from becoming psychiatrists or pediatricians, and 30% would not admit a qualified, "out" applicant to medical school.⁷

Even today, a decade later, these regressive and ignorant views toward bisexuals, gays, and lesbians persist in Canada. During debate on Bill C-33, Dr. Grant Hill, a Reform Member of Parliament, stated, "My specific problem with this bill is that it will produce and allow a promotion of an unhealthy

lifestyle".⁸ Speaking outside the House of Commons, Dr. Hill continued, "These things have been treated as a human rights issue instead of as a medical issue, and as a physician I don't think that's smart." Dr. Hill erroneously used his authority as a physician to perpetuate false myths and stereotypes associated with the LGB community.

Physicians, and future physicians, should be wholly committed to treat all people in a professional manner, regardless of their beliefs, lifestyles, or background. In addition, since a patient's social context and support systems influences his or her health, doctors must be competent in discussing patients' sexual orientation and behaviour with them.

The newly formed Medical Sexual Orientation Issues Group (MedSOIG) at the University of Toronto was created to bring attention to lesbian, gay, and bisexual (LGB) issues in health care. The organization was formed by a group of students concerned that these issues are not being adequately addressed in the medical school curriculum. The group also provides a support network for LGB medical students. Thus far, response to MedSOIG in the Faculty of Medicine has been tremendous.

The need for physicians who are confident in discussing sexual orientation as part of their patient care emphasizes the importance of MedSOIG as a group for all medical students. Future doctors will surely be treating LGB patients in their practices, and failure to communicate effectively with them amounts to providing sub-standard health care. Education about LGB subjects in medicine is a major objective for MedSOIG. The group has already made contributions to the curricula in year one in the courses Health, Illness and the Community course and Art and Science of Clinical Medicine. As stated in the recent JAMA report, "Examining the physical and psychological needs of gay men and lesbians in undergraduate and postgraduate medical education may help physicians feel more confident and less uncomfortable with homosexual and bisexual patients."⁸

MedSOIG has a role to play in helping medical students to feel more comfortable with LGB patients and colleagues in addition to its other mandates. The group consists of people with gay-positive attitudes and as such attaches a face to LGB issues in health. As medical students get to know their gay and gay-positive classmates, the communication that ensues will contribute greatly towards removing the stereotypes and misguided fears that persist concerning lesbians, gays, and bisexuals.

The task of gaining acceptance remains daunting when one considers that for every "out" student in the class, several LGB students remain closeted. These closeted LGB students may be trying to avoid any negative effects their sexual identity may have on their careers or personal lives. The medical community has made gains in its support of progressive attitudes; however, gay, lesbian, and bisexual students still have obstacles to overcome to gain equal footing in the medical profession and to ensure that all patients receive fair and competent care regardless of their sexual orientation.

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In a world which can be described as electronic anarchy, electronic publishing has become the norm and the phrase "buyer beware" takes on added meaning. Anyone with a computer, a modem and some money can publish on the web, which means that everyone traveling the information highway will need to be wary of the validity of any obtained information. In the case of the University of Toronto Medical Journal though, rest assured that each of the articles have been thoroughly peer reviewed and that any future WWW links will be checked with the same diligence. The Medical Journal website, like its paper cousin, is committed to distributing information and articles of the highest quality. So, if you are connected, come and see our website. Welcome to the brave new world.

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Functional MRI: A New Method for Investigating Brain Function

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Abstract

Several methods exist to detect or infer basic brain physiology. Some include computerized tomography, magnetic resonance and positron emission tomography. Until recently, any information on the actual function of the brain had been limited to that deduced from clinical exam - as most imaging techniques were restricted to anatomical visualization. During the 1990s, a greater interest arose in analyzing brain function and dysfunction with focus on the brain's electrical activity. Functional MRI (fMRI) emerged as a new technique to allow scientists to study the function of the brain instead of simply viewing alterations in anatomy. The technique, relying primarily on small differences between magnetic resonance images taken with a stimulus "ON" and "OFF", was able to show areas of brain activation. Further research into the fMRI technique has led to the advent of methods for evaluating actual functional activity in clinical applications and the arrival of a new clinical imaging modality. It is a modality many physicians will see as routine in the near future.

Introduction

Over the past decade, researchers and clinicians in many areas of health and medicine including radiologists, neurologists and psychologists have developed an interest in the use of functional MRI (fMRI) to study brain activity in normal and pathological states. This revolutionary imaging technique highlights brain function by detecting changes in the intrinsic signal from blood that occurs with neuronal activation. These changes are the result of activation induced variations in local cerebral blood flow (CBF), cerebral blood volume (CBV), and blood oxygenation.¹

Prior to the widespread use of fMRI, positron emission

BRYCE HOUGH

tomography (PET) imaging was the modality of choice for studying cerebral activation. fMRI has distinct advantages over PET including greater temporal and spatial resolution.² There is no exposure to ionizing radiation so studies of normal individuals and multiple repeat studies can be performed risk free. As with PET, fMRI compares baseline scans with scans performed during a task highlighting differences in blood flow and blood oxygenation that are produced by specific networks of neurons responsible for performing the task. The premise assumes that local modulation of perfusion is tightly coupled with neuronal activity in the brain.

Early MRI techniques measured changes in signal intensity produced by intravascular contrast (gadolinium-DPTA) passing through capillary beds. Because gadolinium has strong magnetic properties, it causes local distortions of the magnetic field produced by the MRI scanner resulting in localized loss of signal intensity. The movement of gadolinium through the brain microcirculation resulted in a transient flow related drop in signal that could be measured in real time by using a fast acquisition MRI technique called echo-planar imaging.³ Two boluses of contrast were given - one when the patient was at rest, and then a second while the patient was performing a task. Images sets obtained during each bolus were then subtracted showing focal differences in signal intensity in those areas of the brain specifically involved in carrying out the task. The technique was very effective in showing areas of brain activation, but repeat injections of contrast were necessary and access to echoplanar MRI was, and still is, limited. Shortly after the bolus technique was developed, a new method that did not require contrast injections was developed. This technique called the "BOLD (Blood oxygen level dependent) method"^{4,5,6} works by utilizing the difference in the magnetic properties between oxyhemoglobin versus deoxyhemoglobin. Oxyhemoglobin, like water, is diamagnetic and does not alter the magnetic field produced by the MRI scanner. Deoxyhemoglobin, formed when oxygen is transferred to the tissues, is paramagnetic due to the presence of the unpaired electrons in its shell. Deoxyhemoglobin, contained within red blood cells, behaves in the same way as gadolinium creating local distortions in the magnetic field resulting in signal loss.

Although signal differences between resting and active states could be seen with the BOLD method, the magnitude of the effect was quite small. Signal changes in the order of 20% were seen with the gadolinium method, but the BOLD method yielded only 3% differences in signal.² Since the noise inherent in the MR images was on the order of 1%, acquisition of multiple images and rigorous statistical analysis became necessary to identify areas of activation. Initially the validity of the results

using the BOLD method came into question when it was observed that the signal intensity increased in active brain regions suggesting that there was less deoxyhemoglobin present compared to the resting state.^{7,8} This paradox was resolved when it was shown that oxygen delivery (through increased blood flow) far exceeded demand by active neurons.⁹ Post capillary venous blood obtained from active brain regions actually contained more oxygen and less deoxyhemoglobin than blood obtained from resting brain tissues. In spite of the small differences in signal between active and resting tissue, the ability to generate this difference repeatedly simply by having the subject alternate resting periods with task periods allowed acquisition of large numbers of images without the need for repeated contrast injections. The gadolinium method required acquisition of multiple subsecond images to observe the short transit time of the contrast agent through the capillary bed. Since the BOLD method used intrinsic contrast and was independent of capillary transit time, 5 second images could be used allowing implementation on conventional MRI scanners.¹⁰ An important limitation of the technique is that there is a delay between onset of neuronal activation and the subsequent increase in blood flow. The signal changes therefore reflect relatively slow events relative to neuronal activity.

This article will illustrate how fMRI can be used to provide insights into basic brain function, and how clinically relevant information can be obtained in the surgical management of patients.

Methods

1. Patient Set-Up and Protocol

The fMRI technique is more demanding of subjects than clinical scanning. The subject must be capable of completing simple tasks requiring concentration while remaining motionless in the MRI scanner. In order for fMRI studies to be useful, there must be minimal motion between the baseline and active phases in order to reduce artifact when the images are analyzed.¹¹ Shifting the head by as little as a millimeter can result in false activation. Numerous restraint devices have been developed for this purpose.

2. Paradigms

An activation paradigm is designed to assess or localize a specific brain function. A resting phase is compared with a task phase and the two are alternated. For example, the resting phase might consist of a subject holding a ball in his/her right hand. The task phase would consist of repetitively squeezing the ball. This paradigm would

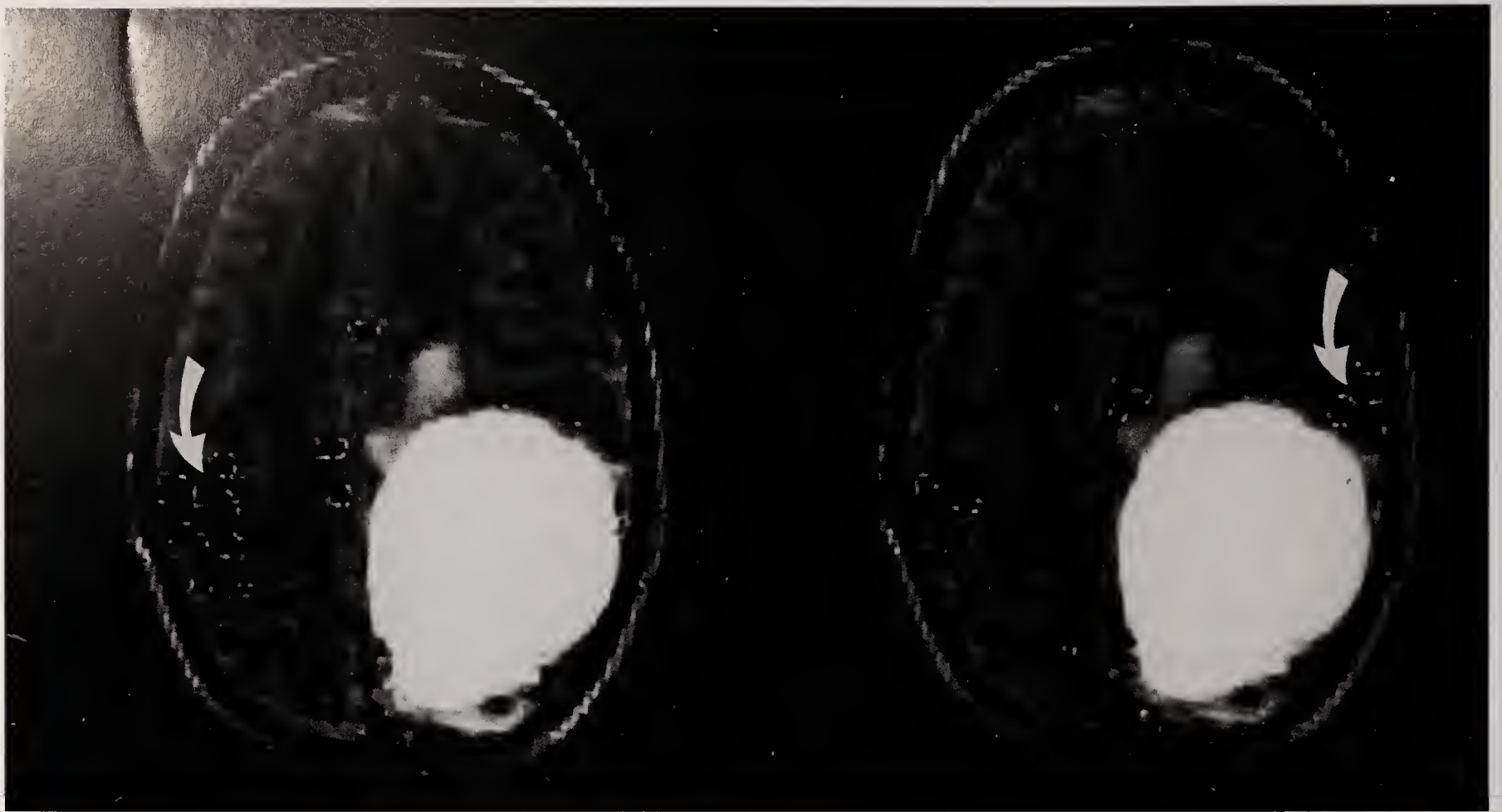


Figure 1: Axial fMRI mapping images taken pre-operatively in patient with low grade glioma. Mapping of motor function using fMRI pre-operatively shows assessment of motor strip. Left image demonstrates patient moving left hand (arrow - motor cortex right hemisphere). Right image demonstrates patient moving right hand (arrow - motor cortex left hemisphere). Note activation of motor strip anterior to tumor in left hemisphere.

outline the left motor strip in the cerebral cortex.¹² Six 5 second images would be obtained for each resting and task period. The resting and task periods would be alternated six times to generate a total of 72 images for statistical analysis.

3. Data Analysis

The most critical and involved step in performing fMRI is the analysis of the images. Most studies involved the generation of hundreds of images at different locations in each subject. All images obtained at a single slice location are identified as either resting or task images. A mean resting image and a mean task image are calculated and compared statistically using a student's t test. If images are acquired on an Echo Planar Imaging system, using the BOLD effect, then a more sophisticated analysis is necessary using a correlation function which takes into account the faster imaging capability of the scanner and the physiologic delay between blood flow and neuronal activation.¹³

Applications of the Technology

Early in the application of the fMRI technology, researchers showed that localized stimulus-dependent activation could be elicited in the visual cortex using

simple paradigms.¹⁴ Next came motor and somatosensory areas which used hand and finger movements.¹⁵ (Figure 1) Finally, more complex paradigms have been developed to study language, memory, and cognition.¹⁶ Researchers at Massachusetts General Hospital in Boston have even been able to demonstrate certain areas of the visual cortex that show sensitivity to shape and form, but not contrast or size.¹⁷

Mapping important cortical functions such as speech and hand motor function in relation to brain tumors prior to resection can lead to improved surgical planning and increased safety of surgery. Scientists are now using increasingly complex paradigms to understand different areas of brain function.

Future

There has been tremendous progress in recent years in many areas of functional brain imaging. The dominant areas of research and use have been pre-surgical mapping of critical areas (Figure 2) and epileptic centres, but exciting new areas are rapidly emerging. fMRI not only allows the study of normal brain processes including problem solving and learning, but will also offer insight into aging and dementia. In addition, mechanisms of injury and recovery - especially post-insult plasticity of the brain - will be elucidated.

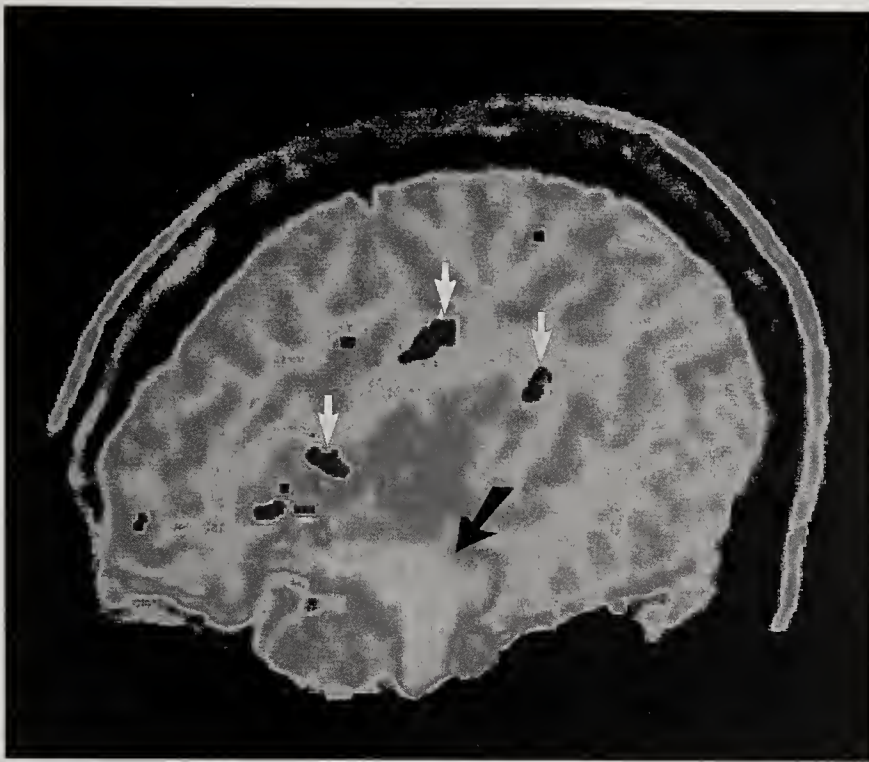


Figure 2: Sagittal fMRI mapping image taken pre-operatively in 11 year old female. Image demonstrates low grade glioma (black arrow) and relationship to Broca's area (Left arrow), Motor area responsible for facial movement in speech (Center arrow) and Wernicke's area (Right arrow).

fMRI will also aid in clarifying mechanisms of disease and pharmaceuticals that we currently do not fully understand. For example, we have much to learn about the identification of seizure foci, spread of seizure activity through the brain, and the mechanism of action of the anti-seizure pharmaceuticals we use.¹⁸ fMRI will assist in clarifying many pieces of this puzzle.

In the clinical arena, fMRI will allow surgeons to map specialized areas of the brain such as the eloquent cortex prior to tumor removal surgery. (Figure 2) This will become increasingly important in the future when minimally-invasive techniques employing small burr holes and electrode heating under MRI guidance will be the surgery of choice for tumor excision.

Conclusion

Because fMRI is noninvasive and does not involve exposure to radiation, it has the advantage of being repeatable in single patients. This will allow clinicians to follow changes in brain function serially over the course of a progressive disease, from injury to recovery or even during the course of pharmaceutical treatment.

First generation studies have shown that fMRI can reliably demonstrate activation in the primary cortices - visual, somatosensory, motor, and auditory. Second generation studies are now exploring the relationship between the MRI signal change in the cortex in relation to the specifics of the task employed in the paradigm. It

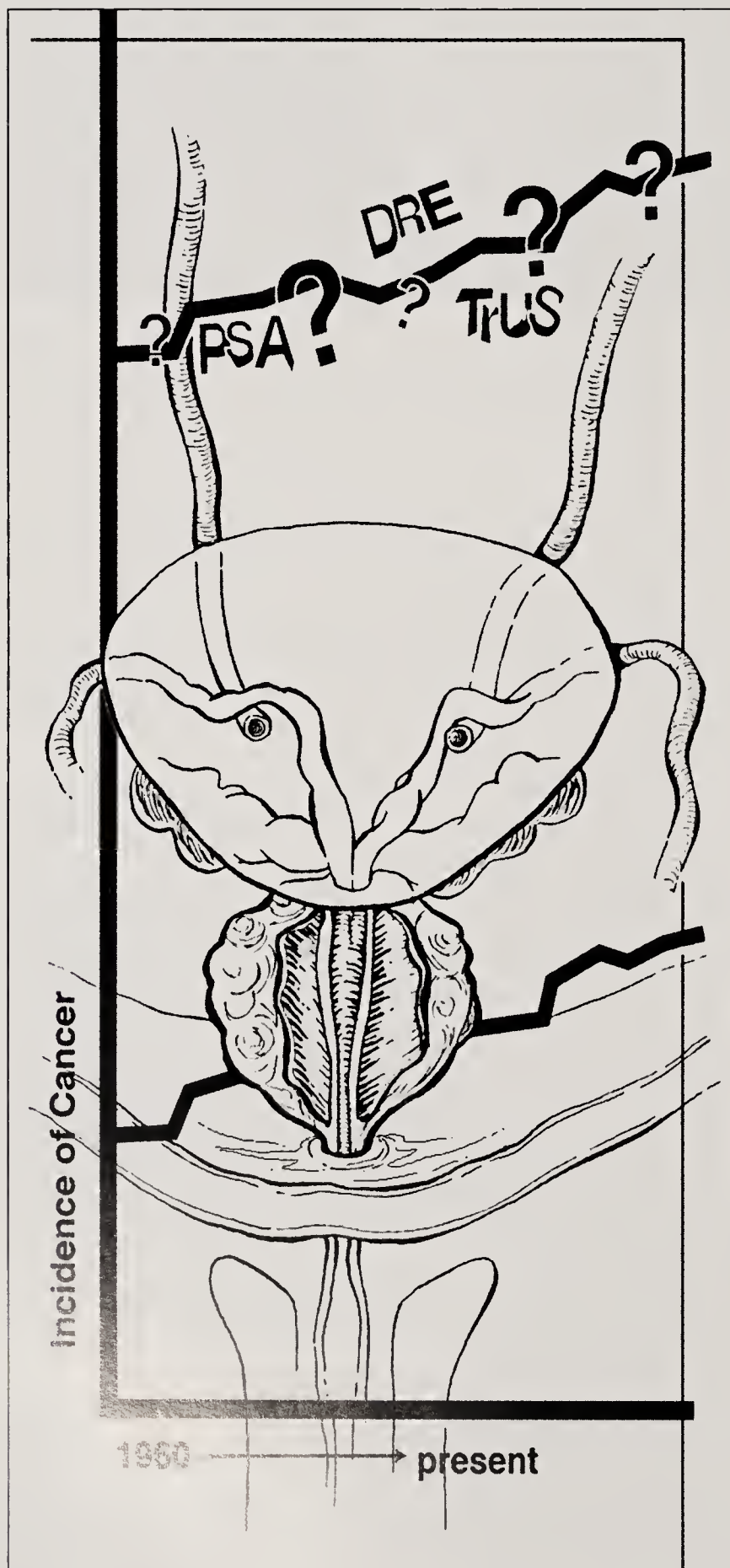
is this increasing complexity that illustrates how fMRI is an exciting and exponentially growing field. The main utility of the technique has been in the neurosciences, however, potential is apparent in all areas of medicine.

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A Review of Prostate Cancer: Risk Factors, Screening, and Diagnosis

Philippe E. Spiess, M.Sc. (9T9), Ali Islam, B.Sc. (9T9), and Asim Ali, B.A.Sc. (9T9)



Abstract

Prostate cancer is the most commonly diagnosed cancer and second leading cause of cancer deaths in North American men. It is estimated that by the year 2000, the incidence of prostate cancer will increase by another 90% and deaths from this malignancy will increase by 37%. Despite the intensive efforts over the last decade to unveil the etiology of prostate cancer, the pathogenesis of this disease remains poorly understood. Epidemiological studies have shown that age, race, family history, and possibly vasectomy may constitute risk factors for prostate cancer; however, their importance remains to be elucidated. Currently, digital rectal examination, transrectal ultrasonography, and serum prostate specific antigen measurements are the principal screening tools for prostate cancer. A confirmation of the diagnosis is usually made by prostatic biopsy. The aim of this review is to examine the diagnostic techniques and screening programs currently used in the treatment of prostate cancer.

Résumé

Le cancer de la prostate est le plus commun des cancers diagnostiqués chez les hommes, ainsi que la deuxième cause la plus importante de mortalité en Amérique du Nord. Il est estimé que d'ici l'an 2000, le taux de cancer de la prostate augmentera de 90% et le taux de mortalité de à sa malignité augmentera de 37%.

Malgré d'intenses efforts durant ces dix dernières années, pour dévoiler l'aetiology du cancer de la prostate, la pathogénie de cette maladie reste très peu comprise. Des études épidémiologiques ont de montré que l'âge d'un individu, sa race, son antécédent familial ainsi que la possibilité d'avoir subi une vassectomie antérieurement

peuvent contribuer aux facteurs de développement du cancer de la prostate bien qu'il reste à déterminer l'importance que ces critères portent à l'évolution de la maladie.

A ce jour, la détection du cancer de la prostate consiste de l'utilisation de touché rectale, examination par ultrason, et mesure de PSA. Si le diagnostique de cancer de la prostate est soupçonné par ces méthodes, une biopsie prostatique est normalement faite.

Le but de cet article est d'étudier les techniques de diagnostique ainsi que les méthodes de détection disponibles pour le cancer de la prostate.

Introduction

Structure and function

The prostate gland is a walnut-sized glandular organ located at the neck of the urinary bladder surrounding the urethra. It has an external fibroelastic layer, which projects inwards to form septae. These divide the prostate into five lobes: anterior, posterior, medial, and two lateral lobes. It is comprised of epithelial, stromal, and smooth muscle tissues. The smooth muscle enables it to regulate urinary flow from the bladder and the ejaculation of seminal fluid.

The prostate gland has both exocrine and endocrine functions. The secretions of the prostate contain various enzymes, lipids, ions, and amines. These secretions maintain sperm viability, provide nutrition for spermatozoa, and have anti-bacterial activity.¹ The endocrine role of the prostate gland is to convert testosterone to dihydrotestosterone.

Pathological changes

The three cell-types present in the prostatic epithelium are: secretory luminal, basal, and endocrine-paracrine cells.² The basal cell layer is the proliferative component of both normal and hyperplastic epithelium. When transformed stem cells of the basal cell layer gain secretory luminal characteristics under androgenic stimulation, prostate cancer may result.

Epidemiology and risk factors for prostate cancer

In Canada, prostate cancer is responsible for 20% of new cancers and 12% of cancer deaths in men.³ There were approximately 244,000 new cases of prostate cancer diagnosed in North America in 1995.⁴ In this same study, it was estimated that by the year 2000, the inci-

dence of prostate cancer will increase by 90% and deaths from this malignancy by another 37%. The increased incidence may be partly explained by increased screening and by incidental findings of prostate cancer on transurethral resection of prostate (TURP) for benign prostatic hyperplasia (BPH).

Risk Factors

The etiology of prostate cancer remains poorly understood despite intensive investigation over the past decade; however, certain risk factors have been identified including age, race, family history, and possibly vasectomy.

Age

In a study by Klein, the incidence of prostate cancer increased with age.⁴ The prevalence at the time of autopsy was 30% in men over age 50 and 70% in men in their 80s.^{4,5} A recent study has shown that the rate of age-adjusted incidence of invasive prostate cancer rose significantly from an increase of 8% in 1989, to 33% in 1990, and 72% in 1991.⁶ This same study showed that the rate of diagnosis increased for all ages over 50 with the most marked increase in men between 75 and 84 years of age.

Race

There are large geographic variations in the incidence of prostate cancer, ranging from more than 1 per 100,000 to 100 per 100,000.⁷ There are also variations between racial groups within the same geographical location. This is most evident in the United States, where African-Americans have a higher age-specific incidence and a higher death rate from prostate cancer than Caucasians. It was reported in 1995 that the lifetime risk of dying of prostate cancer is 4.3% in African-Americans versus 2.6% in Caucasians.⁷ The higher death rate in African-Americans has never been adequately explained. A study in 1989 of 152 males aged 50 years or younger indicated that premalignant lesions and incidental carcinomas of the prostate occurred with equal frequency in both races.⁸ As well, the cancerous foci were of similar size and occurred as early as the third decade in African-Americans and Caucasians, suggesting that both races were equally prone to develop prostate cancer.

Family history

Family history is another risk factor for prostate cancer. An epidemiological study in 1990 demonstrated that a

man's risk of developing prostate cancer is approximately twice that of the general population if he has a first-degree relative with the disease and almost 9 times as great when both a first and second degree relative are affected (Table 1).⁹

Table 1 Risk of developing prostate cancer according to family history	
Relative(s) affected	Relative risk
One second-degree	1.7
One first-degree	2.0
Two first-degree	4.9
One first and one second degree	8.8
Three or more first degree	10.9
Adapted from Steinberg et al. ⁹	

A number of families in which a hereditary form of prostate cancer occurs have been identified. They are characterized by an early age of onset as well as by autosomal dominant inheritance. This hereditary form of prostate cancer should be suspected if prostate cancer occurs in multiple generations or in multiple family members, particularly if the age of onset is less than 55. In such families, men have an approximately 50% risk of getting prostate cancer in comparison to a 13% risk in the general population.¹⁰ Genetic studies have shown that the gene responsible for hereditary prostate cancer is highly penetrant with 88% of gene carriers developing prostate cancer by age 85. Hereditary prostate cancer does not appear to be associated with other forms of cancer.¹¹

Vasectomy

Several studies have demonstrated a higher risk of prostate cancer in men who have had a vasectomy. The relative risk of developing prostate cancer has been suggested in several studies to be approximately 1.5 times higher in patients who have had a vasectomy than in the general population.^{12,13} The exact nature of the association between vasectomy and prostate cancer has not been elucidated. However, the American Urological Association recommends that urologists and other physicians discuss this possible risk with those men considering vasectomy.

Diagnosis and Presentation of Prostate Cancer

Signs and symptoms

The most common symptoms that patients present with are urinary urgency, nocturia, increased frequency, and hesitancy which result from a urinary tract obstruction due to an enlarged prostate gland.¹⁴ (Table 2)

Table 2 Summary of diagnosis and presentation of prostate cancer
Common symptoms Urinary urgency, nocturia, increased frequency, and hesitancy
Signs Asymmetry, change in contour and induration of prostate on digital rectal examination
Other findings on investigation Hypoechoic lesions on transrectal ultrasound Elevated serum PSA levels Detection of malignancy upon biopsy

It is difficult to determine if these symptoms are caused by cancer or by benign prostatic hyperplasia (BPH), except that symptoms due to cancer can have an abrupt onset. Other signs and symptoms of prostate cancer that should be considered include the acute onset of impotence, as it may result from the malignancy involving periprostatic tissue. Patients presenting with metastatic prostate cancer may complain of back pain secondary to vertebral metastasis. Additionally, a small percentage of patients may initially present with acute urinary retention caused by bladder neck obstruction, bilateral hydronephrosis caused by periaortic lymph node enlargement, or spinal cord compression caused by epidural extension of the carcinoma.

The suspicion of cancer increases if induration, changes in contour, and/or asymmetry of the gland are detected by digital rectal examination (DRE). The positive predictive value of DRE ranges from 22% to 39% depending on the patient population.¹⁵ Abnormal DRE's should be followed up by transrectal ultrasonography (TRUS) and serum PSA determination.

Transrectal ultrasonography

TRUS allows non-invasive visualization of the prostate. It is used to detect hypoechoic lesions suggestive of cancer and also helps to guide prostatic biopsy. But not all cancers are hypoechoic and small, early stage tumours are difficult to resolve. Thus, the positive predictive value ranges from 15% to 36% if TRUS is used alone.¹⁵ In this study, the positive predictive value was improved to 38% when used in conjunction with DRE.

Prostate specific antigen

PSA, a serine protease, is produced by epithelial cells of the acini and ducts of the prostate gland. It is involved in degrading the seminal coagulum that is formed at ejaculation. Also, in recent years it has shown usefulness as a marker for prostate cancer. Measurements of PSA are non-invasive and relatively inexpensive. The specificity of PSA testing for detection of prostate cancer is low because BPH and prostatitis can elevate PSA levels. The positive predictive value of this test ranges from 28% to 35% when used alone.¹⁶

Recently, there has been a great deal of controversy as to what is considered an elevated PSA level. Many have considered a serum PSA above 4 ng/ml (by Hybritech assay) as elevated whereas others such as Oesterling¹⁷ have suggested using age-specific PSA cutoff levels to increase the sensitivity of this screening method in younger people and its specificity in older patients (Table 3). However, it is estimated that using these age-adjusted PSA levels, 5 to 15% of carcinomas in patients 60 to 69 would be missed.¹⁸

Table 3
Age specific normal PSA levels

Age	Normal PSA range (ng/ml)
40-49	0-2.5
50-59	0-3.5
60-69	0-4.5
70-79	0-6.5

Adapted from Oesterling et al.¹⁷

As well, there have been other approaches taken to improve the specificity and to reduce the number of prostatic biopsies required to diagnose prostate cancer. One such approach is to define the expected rate of increase

in PSA with the age-related increase in prostatic size (known as "PSA velocity"). Clinical studies have suggested that an increase in PSA of more than 0.75 ng/ml per year would be suggestive of prostate cancer whereas slower rises in PSA may be more suggestive of BPH. It has been suggested that the implementation of PSA velocity as a screening tool would increase the specificity of the test to more than 90%. In other studies, it was suggested that any increase in serum PSA of more than 20% per year should warrant taking a prostatic biopsy.¹⁹ The disadvantage of both these approaches is that it would require the repeated measure of serum PSA at 1 to 2 year intervals.

Another approach is the measurement of bound and unbound PSA in the serum as it has been shown that men suffering from BPH have higher amounts of unbound PSA whereas those with prostate cancer have more PSA bound to antichymotrypsin.⁴ Initial reports suggest that an unbound/bound PSA ratio of less than 0.15 would be more suggestive of cancer and would require performing prostatic biopsies.

Biopsy

If prostate cancer is suspected based on findings of DRE, PSA, and TRUS, biopsy of the prostate is warranted. Both fine needle aspiration (FNA) and ultrasound-guided core biopsy are highly accurate in diagnosing prostate cancer.²⁰ In a recent study, it was shown that the sensitivity and specificity of FNA were 96.5% and 97.8% respectively, versus 92.2% and 99.3% for core biopsy.²¹ However, the TRUS-guided technique can better estimate the extent of the tumor.

In addition, incidental findings of prostate cancer are obtained in a significant number of patients when tissue samples are examined following TURP for treatment of BPH.¹⁵

Screening for Prostate Cancer

Screening for prostate cancer remains controversial as no studies have been able to document a decrease in the mortality rate in screened patient populations. However, it must be noted that PSA testing only began to be used in screening programs about 5 years ago whereas most survival analyses are usually measured with 10 and 15 year survival rates. As such, the effectiveness of screening programs using PSA levels as a screening tool is uncertain at the present time. Hopefully, this will change when clinical studies such as the National Cancer Institute's screening trial for prostate cancer release their results within the next 5 to 10 years.

The most commonly used screening procedures include DRE, serum PSA, and TRUS. In a recent multicenter study in which 6000 men were screened, the overall detection rate was highest with PSA testing (4.6%), followed by DRE (3.2%).²² It was also shown that the combination of an elevated PSA, abnormal finding on DRE, and abnormal TRUS carry a combined positive predictive value of 55%. However if convenience, patient comfort, and variability in ultrasonographic findings are considered, the combination of DRE and PSA testing may be the most cost-effective.

Conclusion

Although it has yet to be shown that screening reduces the mortality from this malignancy, several studies have indicated that screening detects a higher proportion of patients with organ-confined tumors than in non-screened patients.^{23,24} The long-term survival rates are better for organ-confined cancers. In a study by Catalona,²⁵ a series of 2000 men newly-diagnosed with prostate cancer were screened by DRE, a single measurement of serum PSA, and serial measurements of PSA. It was determined that the use of serial PSA measurements detected the highest number of organ-confined cancers whereas use of DRE alone had detected the least number of locally confined tumors.

The question of whether or not men should be screened for prostate cancer remains one of the most commonly debated points in urology. The U.S. Preventive Services Task Force, the Canadian Task Force on the Periodic Health Examination, and the Canadian Urologic Association recommend against PSA screening.^{16,26} However, the American Urological Association, the American College of Surgeons, and the American Cancer Society all suggest that men with no risk factors for prostate cancer undergo annual DRE and PSA testing starting at the age of 50. However, those men with risk factors including age, race, family history, and vasectomy are advised to begin screening at age 40. There is no set age at which screening should be stopped, but it has been suggested that if a patient has a less than 10-year life expectancy or is unlikely to be a candidate for therapy, even if prostate cancer is discovered, then the option to stop screening should be strongly considered.^{27,28}

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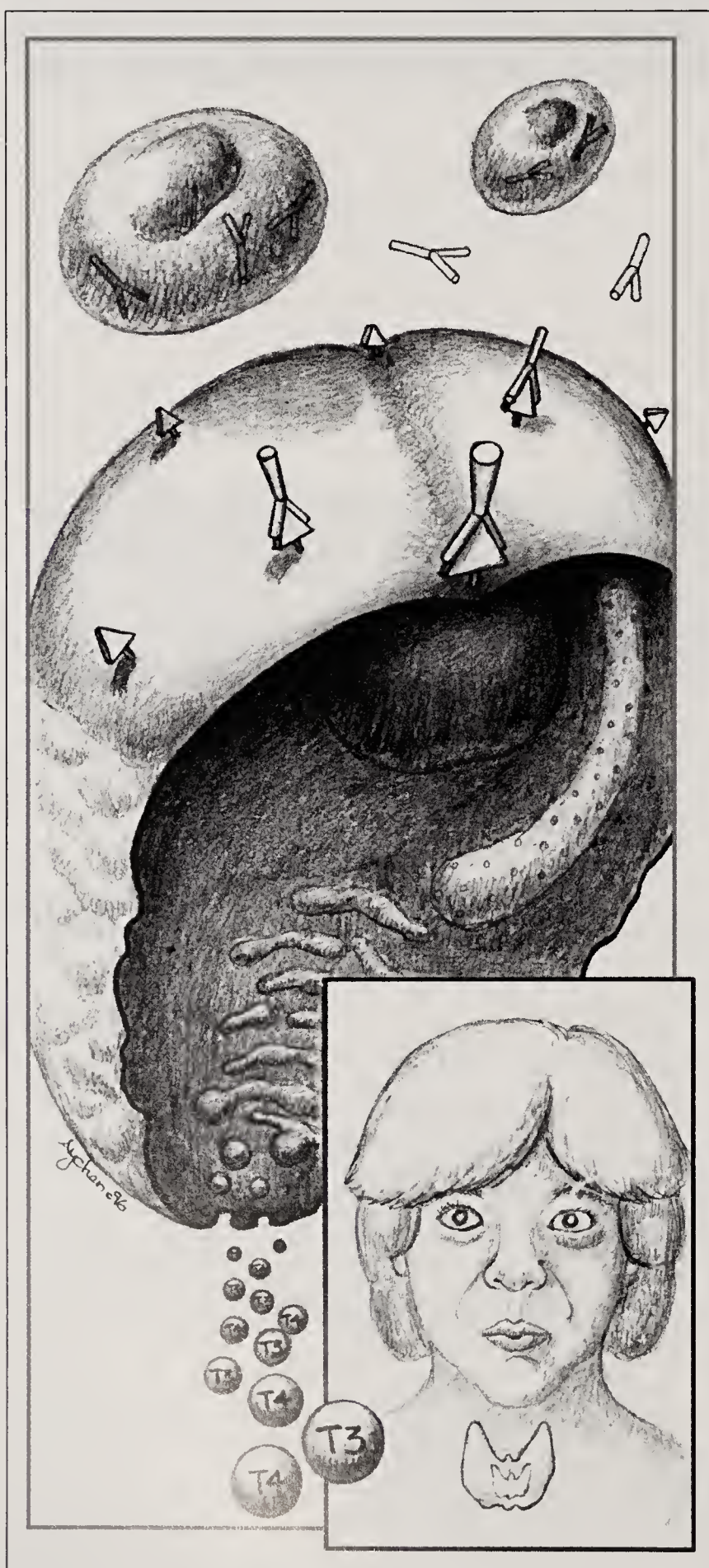
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The Current Management of Graves' Disease

Sanam Shorey, B.Sc. (9T9)

Special thanks to:

Dr. Paul Walfish, M.D., F.R.C.P.(C.), F.R.S.M., Division of Endocrinology and Metabolism and Head and Neck Oncology Program of Mount Sinai Hospital, Toronto, Canada



ALICE CHEN

Abstract

Graves' disease (GD) is an autoimmune disorder of the thyroid gland characterized by hyperthyroidism and diffuse goitre with occasional ophthalmopathy and dermopathy. While there are various disorders that result in hyperthyroidism, Graves' disease is by far the most common, presenting itself more often in women than in men and capable of occurring at all ages. The clinical consequences resulting from Graves' disease may be quite severe and therefore it is essential that the diagnosis and treatment of this condition be achieved as soon as possible.

In this paper, focus will be placed on a case report of a patient with Graves' disease, commenting on the signs and symptoms, investigative procedures for diagnosis, and current forms of treatment used in practice with emphasis on the relative advantages and disadvantages of each.

Introduction

Graves' Disease (GD) is mediated by IgG autoantibodies that bind to thyroid-stimulating hormone (TSH) receptors located on thyroid follicular cells.¹ The major forms include: (1) thyroid stimulating antibodies (TsAb), which act to further stimulate intracellular adenylate cyclase activity, increasing cAMP and resulting in the increased release of thyroid hormones into circulation; and (2) TSH binding inhibiting immunoglobulin (TBII), which competitively binds to the TSH receptor mimicking the action of TSH.^{2,3}

In clinical practice, it is common to observe cases of GD in one family and in successive generations, suggesting a genetic etiology. To support this, researchers have shown certain MHC class II alleles to occur more frequently in patients with GD compared with healthy controls.^{4,5} Other factors thought to be involved include immuno-

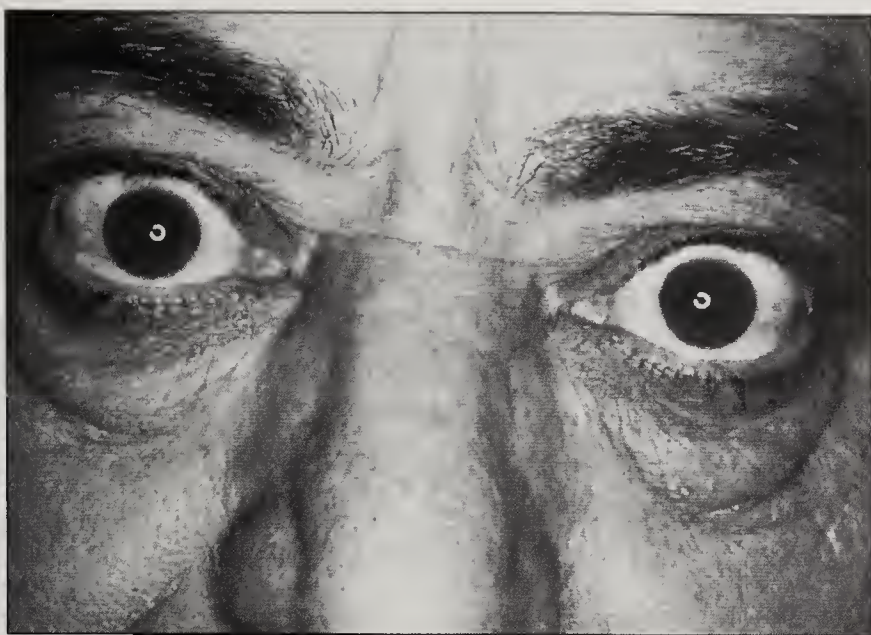


Figure 1: A patient with mild ophthalmopathy due to Graves' Disease. Note the prominence of the eyes, infraorbital puffiness and the widened palpebral fissure.

logical abnormalities such as reduced T-cell suppressor function. This may allow helper T-lymphocytes to stimulate B-lymphocytes to produce immuno-globulins directed against the thyroid gland.³

Among the causes of spontaneous occurring thyrotoxicosis, GD is the most common. Its frequency as the cause of thyrotoxicosis ranges from about 60-90% in different regions of the world. Other less common types of hyperthyroidism include toxic nodular goitre (TNG), where one or more nodules in the thyroid gland become overactive, thyroiditis, radiation injury to the gland, thyroid carcinoma, and the exogenous intake of thyroid hormone.^{6,7} Of interest is that GD, unlike TNG, is caused by the hyperfunction of the entire gland, not by specific nodules, and it is often referred to synonymously as Toxic Diffuse Goitre.⁸

The excessive serum concentrations of thyroid hormones resulting from GD targets all vital organs of the body, resulting in many signs and symptoms (Table 1). Approximately 80% of patients have clinically evident ophthalmopathy with exophthalmos (abnormal protrusion of the eyeballs) as their key feature. Much rarer is the occurrence of pretibial myxedema (localized thickening of the skin over the lower tibia) and thyroid acropachy (thickening of the extremities), present in less than 2-3% of patients with GD.^{9,10} If GD goes untreated, the resulting thyrotoxicosis may become life-threatening. The case below describes a patient diagnosed and treated for GD.

Case Report

A 39 year old Caucasian female first presented with palpitations, irritability, sweating, heat intolerance, and

generalized fatigue of 2 weeks duration suggestive of new onset of hyperthyroidism. The patient also mentioned a 10 lb drop in weight over the last month despite a good appetite. Assessment revealed no family members with diabetes or thyroid problems except for her mother who had GD. Past health and functional inquiry were unremarkable. There were no previous pregnancies, and regular menses was noted. She was on no current medication.

Physical examination revealed a tense nervous female at 5'10", weighing 120 lbs, with a blood pressure of 140/70 mmHg right arm seated and a pulse of 105 beats/min and regular. The thyroid gland was diffusely enlarged on palpation at approximately 40-45 grams (normal 15-20 gms) with the right lobe being more prominent and no nodularity detected. There was no cervical lymphadenopathy or overlying carotid bruits. On ocular examination, there was mild infraorbital puffiness with lid lag and lid retraction. There was also slight proptosis in both eyes (Figure 1). No diplopia was evident and eye movements were normal. Exophthalmometer readings at base 93 were Right 22 and Left 24 (Normal < 20 mm) and there was no definitive enlargement of the rectus muscles. Achilles reflex was 3+ and symmetrical. Skin was warm and moist and a fine tremor of the outstretched hand was noted.

Blood tests revealed high serum T4 levels at 190 nmol/L (normal 60-155), high serum T3 levels 2.9 nmol/L (normal 1.1-2.6), accompanied by suppressed TSH of <0.03 mIU/l (normal 0.5-4). Serum anti-thyroid antibody

Table 1	
Symptoms and Signs of Graves' Disease	
Symptoms	Signs
Nervousness	Tachycardia
Palpitations	Systolic hypertension
Irritability	Tremor
Heat intolerance	Warm moist skin
Fatigue	Lid lag and retraction
Weight loss	Goitre
Increase in bowel movements	Brisk reflexes
Decrease in menstrual periods	Localized myxedema +
Eye irritations *	Acropachy +
* mild cases: redness, sensation of dryness, mild proptosis Severe cases: diplopia, diminished vision, extreme proptosis + very rare occurrence (<2-3%).	

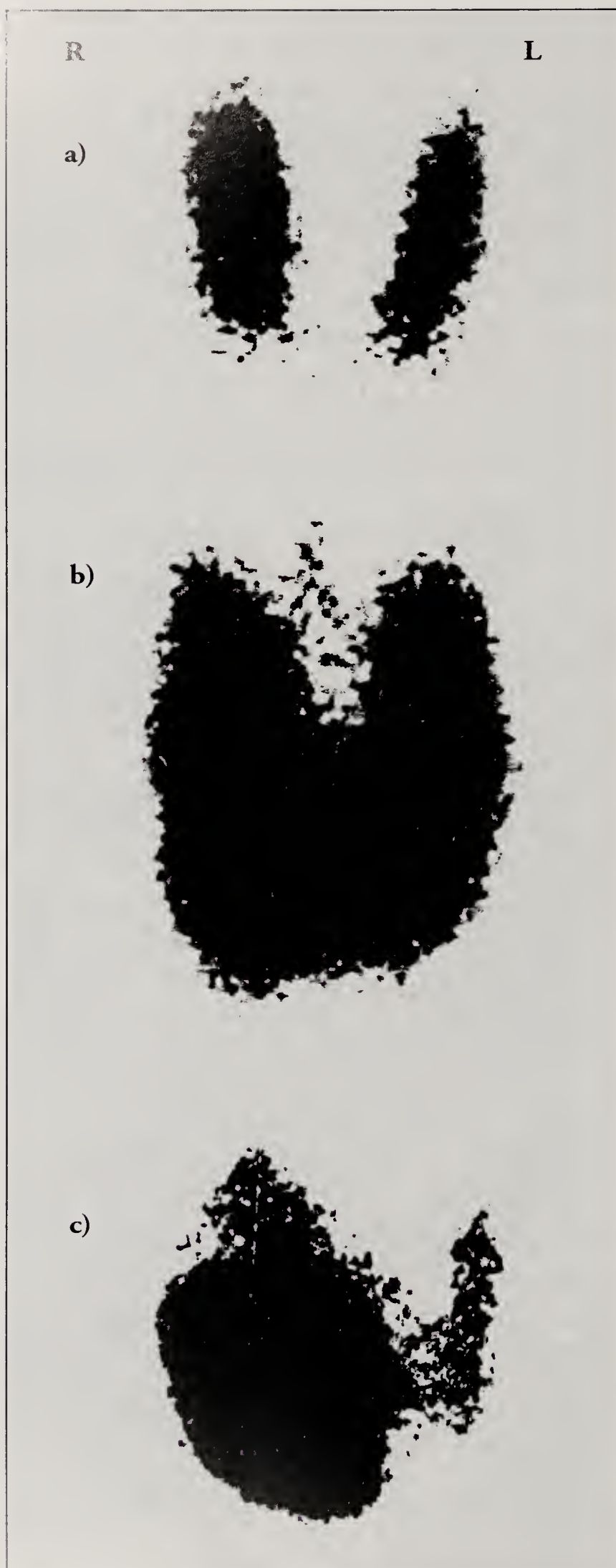


Figure 2: *Thyroid Scan demonstrating (a) a normal thyroid gland; (b) an enlarged gland with a pyramidal lobe and diffusely increased tracer uptake in a patient with GD; (c) shows a foci of increased tracer uptake in the right lobe in a patient with Toxic nodular goiter.*

titers were weakly positive for anti-thyroglobulin (A-Tg) and anti-microsomal (A-Mc) autoantibodies. At this time, a thyroid scan was ordered which showed a diffusely hyperactive gland with an elevated 24hr-radioactive iodine uptake (RAIU) at 50% (normal <25%) (Figure 2a, 2b). These observations, in conjunction with the presence of a positive TBII value at 51% (normal <8%) were confirmatory of GD. Short-term propranolol (Inderal), a beta-blocker, was instituted and propylthiouracil (PTU), a thyroid hormone blocker, was initiated for 9 months before receiving radioactive iodine-131 at an ablation dosage of 25.5 mCi to destroy the thyroid gland.

The patient was subsequently started on long-term levothyroxine (Synthroid) replacement for post-radioactive induced hypothyroidism. When last reviewed, her condition had stabilized considerably, and she was clinically well with resolution of her mild ophthalmopathy.

Investigations

In practice, once the question of GD has been raised, laboratory studies must be performed to confirm the diagnosis. Blood tests provide the starting point with focus primarily on total serum thyroxine (T₄) and serum TSH levels. High values of T₄ accompanied by suppressed TSH confirms hyperthyroidism, but not its cause.¹¹ Causality is aided by a thyroid scan. The procedure involves the patient ingesting a small amount of radioactive material, usually I¹²³, which is taken up by the thyroid gland. The resulting scan determines the pattern and quantity of radioiodine uptake. In GD, the scan typically shows a symmetrically enlarged gland with homogeneous tracer distribution and a prominent pyramidal lobe.¹² This pattern helps differentiate GD from TNG which is shown in Figure 2c. The 24hr RAIU is usually very high in GD (>25% of the administered dose) and helps differentiate from patients with silent or post-partum thyroiditis, a condition which normally has low RAIU values.¹³

Determination of antithyroid antibody titers provides further supporting evidence for GD. More than 95% of patients have positive A-Mc titers (antibodies directed against thyroid peroxidase) and about 50% have positive A-Tg titers (antibodies directed against thyroglobulin).¹⁴ Testing for TBII, which has been detectable in about 60-80% of new GD patients,¹⁵ has also been useful with a positive test supporting the diagnosis. The combination of the above procedures may not always be warranted in the diagnosis of GD, but is highly recommended.

Treatment

Three forms of primary therapy for GD are in common

use today: (1) blocking of hormone synthesis by antithyroid drugs; (2) radioactive iodine thyroid ablation; and (3) partial thyroidectomy.

(1) Antithyroid Medication

Methimazole (Tapazole) and propylthiouracil (PTU) are the mainstays of antithyroid drug therapy.¹⁶ Their principal action is the inhibition of thyroid peroxidase, an enzyme responsible for organification of iodine and coupling of iodothyronines, which are essential for thyroid hormone synthesis. In addition, PTU inhibits the peripheral monodeiodination of thyroxine to triiodothyronine.¹⁷ Therapy is usually prescribed for 8-14 months in attempts to achieve remission. Reports on long-term remission show conflicting results ranging from 10-75%¹⁸⁻²⁰ with higher remission rates associated with longer treatment²¹ and higher doses.²² Drug therapy offers an opportunity to avoid damage to neck structures due to surgery and radiation. However, difficulties may include the need to be compliant with medication, the frequent visits to physicians, and the chance of hyperthyroidism recurring. Side effects range from allergic reactions, nausea and loss of taste, present in less than 5% of patients, to severe complications, such as reversible agranulocytosis, in less than 1% of patients.²³ Determining which patients should receive antithyroid therapy has been a controversial issue; however, there appears to be a consensus for treatment to be used for all uncomplicated patients below age 55, especially in adolescents and in pregnant women.

(2) I¹³¹ Ablation

In many clinics, I¹³¹ ablation is the main choice of therapy for GD. It is commonly employed in patients above age 21, especially if antithyroid drugs fail to control the condition. It is contraindicated in pregnant or lactating women and in adolescents.²⁴ The procedure involves the ingestion of a small dose of I¹³¹ in the form of a capsule. The radioactive iodine is taken up by the thyroid cells very readily in GD (primarily due to the high RAIU) where it acts to destroy the thyroid parenchyma. Prior to the procedure, patients on antithyroid medication are advised to cease their medication 2 weeks before, and to commence on a low iodine diet 7 days before admission (the latter allows radioactive iodine to enter the thyroid gland with minimal competitive interference from its non-radioactive form). Individuals given a high dose of I¹³¹ (usually > 30mCi) are kept in the hospital for a few days whereas those with lower doses are recommended to avoid close contact with others for the same period of time for precautionary reasons.

Radioiodine ablation essentially cures hyperthyroidism and decreases the size of the thyroid in virtually all patients.^{25,26} Once euthyroidism occurs, hyperthyroidism rarely recurs.²⁷ The procedure is quick, easy, and avoids surgery. The fear of developing significant carcinogenic, leukemogenic, or teratogenic effects in the doses used to treat GD is unfounded.^{28,29} The major drawback of radioactive treatment is the high incidence of hypothyroidism³⁰ and patients are subsequently told to commence on long-term levothyroxine (Synthroid) therapy. However, thyroidologists often agree that it is much easier to control hypothyroidism than hyperthyroidism.

(3) Partial Surgical Thyroidectomy

Surgery was the main form of therapy before the 1950's; however, it has now been largely replaced by I¹³¹ treatment. In a survey performed by the American Thyroid Association, a consensus among 235 clinically active members showed that 69% use radioactive therapy as their first choice and 30% prefer antithyroid medication, whereas surgery was chosen by only one respondent.³¹ Partial thyroidectomy involves the surgical removal of most of the thyroid from the patient. The procedure is primarily performed on patients with large and cosmetically disfiguring goitres, on patients where compliance to medication is a problem, and on those who prefer the rapidity and excellent chance of first time cure.¹⁵ Patients prior to surgery are placed on antithyroid medication to render them in a state of euthyroidism by the time the surgery is performed. Seven to ten days before the operation a few drops of non-radioactive iodine (either Lugol's iodine or a saturated solution of potassium iodide) is administered orally, which reduces blood supply to the thyroid gland, making the surgeon's task easier.³² Pre-operative preparation with beta-adrenergic blockers alone or with iodine can also be used.³³ Post-operative complications include hypoparathyroidism and hoarseness (recurrent laryngeal nerve damage), but these are very rare.¹⁵ Also, there is a high incidence of recurrent hyperthyroidism if too much tissue is left and a high incidence of post-operative hypothyroidism if too much thyroid tissue is excised; the latter is treated by long-term levothyroxine (Synthroid) therapy.

Adjunctive Therapy

Beta-adrenergic blockers such as propranolol (Inderal) are often instituted to provide symptomatic relief for GD. Such therapy has very little effect on the disease process.³⁴ The drugs act by blocking the action of circulating thyroid hormone on body tissues. Beta-blockers are ceased when euthyroidism is achieved.

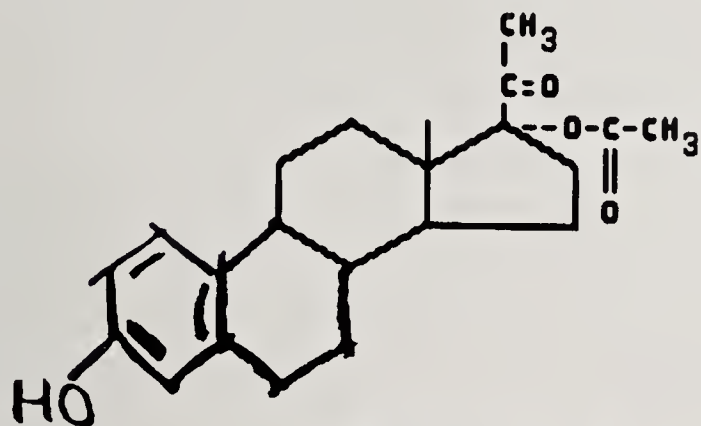
Summary

GD is one form of hyperthyroidism, which in general can be easily diagnosed with the knowledge of the clinical signs and symptoms and the aid of laboratory investigations. Presently, radioiodine therapy is the preferred method to treat GD; however there are certain circumstances when the other two modes of treatment are employed. Palliative therapy with beta-adrenergic blockade is very useful in many patients in providing symptomatic relief. Although all types of treatment are easily performed and provide gratifying results, the therapy is directed away from the immunological cause of GD. It would be interesting to see if such a therapy can be made possible and used successfully in the future management of GD.

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Ethical Dilemmas of Clinical Clerks

Vincent Lam, B.Sc. (9T9)



KIMBERLEY PETER

Abstract

The past 25 years have seen ethics assume a greater importance in medical curricula. There has been a recognition that students should not be expected to 'pick up' ethics on their own, but should receive training in the complex moral problems that physicians face.¹ But does ethics instruction deal with problems that students face as students?

Ethics and Medical Students

Most practical ethical training focuses on interactions between physicians and patients. While it is true that medical students are learning to be physicians, they find themselves in the sometimes awkward position of being neither lay person nor doctor.² This situation may require additional skills to deal with ethical problems as clinical clerks. Meanwhile, most theoretical ethical training is rooted in principles of rights and obligations, non-maleficence, autonomy, justice, and the ways in which these can play against each other.³ These are important ideas. Clinical clerks, however, may face insidious and immediate clinical ethical problems that do not fit into this framework of conflicting principles.⁴ This paper will examine some of the ethical problems that clinical clerks may face and will discuss some directions for addressing these problems.

Clinical Clerks' Intermediate Positions

Clerks have an intermediate position with respect to knowledge, status, and motivations. While they have some medical knowledge, it is not complete enough for them to practise medicine. They have some status as health care quasi-professionals, but do not have the independence that a staff physician has. Clerks are motivated to care for patients, but are also motivated by desires for clinical experience and career advancement. Each of these intermediate positions can create situations of sub-

tle, but very real ethical conflict. These factors are integrally linked with one another. However, this paper will address knowledge, status and accountability, and motivations separately to emphasize how each may create ethical difficulty. This discussion will be grounded by reference to cases described by Christakis and Feudtner.²

It should be noted that other members of the hospital medical team such as nurses and members of the allied health professions may experience similar ethical challenges. This discussion may overlap with their concerns. For clarity, this paper only deals directly with the ethical concerns of clinical clerks.

Intermediate Knowledge

Case 1

"I had interviewed and examined a patient when he was first admitted to the hospital for his intractable cough, and I had gotten to know him very well. We respected each other. When I learned that the biopsy of a lung nodule showed an undifferentiated carcinoma, I was very upset, but I wanted to be there when he was told. When I asked my resident who would inform the patient of the biopsy results, he instructed me that no one on our team was to say anything. Instead, the oncologists would tell him, since they knew more about the disease and had more experience telling patients bad news. For the next two days the patient repeatedly asked me if I knew the results, and with many misgivings I told him 'no'. When he finally learned, he was very angry that I had kept the truth from him - and I couldn't blame him."

Knowing about the carcinoma, this clerk felt a personal obligation to inform the patient. However, this link between knowledge and an obligation to act has another perspective. Within a medical team, greater knowledge translates into greater decision making power.² It is expected that those with less knowledge will defer to those with more knowledge, presumably because they will be able to make better decisions and act more effectively. In this case, the resident was more knowledgeable about hospital protocol, and the oncologists were more knowledgeable about carcinoma. The clerk was left trapped between a personal obligation to inform the patient and an obligation to defer to greater knowledge.*

Partial Status and Partial Accountability

Here, status will refer both to the health care team members' professional and personal approval of a clerk. Accountability will refer to the personal link that one feels for the consequences of his/her actions or inaction.

On a medical team, an ethos of 'teamwork' exists.² A

'team player' is one who performs his/her tasks as required and requested, cooperates with the decisions of superiors, and who is willing to set aside personal concerns for the smooth functioning of the team. To learn to work within a team is a crucial skill for any clerk to acquire. It should also be noted that such integration may be an important determinant of approval or status. Approval results in favourable evaluation and personal recommendation, which may play an integral role in a clerk's career.

A physician often assumes a central role in decision making. His/her role as a team player is to consult other health care professionals, make decisions concerning care delivery, and to bear responsibility for the consequences of his/her decisions. A physician's professional status derives largely from his/her ability to perform these tasks well. A clerk is more bound to being a dependent element in the team. Clerks perform some of the tasks of physicians, and may be willing to assume more. Clerks, however, do not derive professional status from 'directing' situations. As such, they must acquire status as a more peripheral element of the team.

Case 2

"My intern asked me to get an informed consent from a patient for a procedure. I had seen this procedure done before, but really felt that the consent should be obtained by the intern. Nevertheless, I knew he thought he was doing me a favor, giving me something meaningful to do, even granting me the honor of obtaining a consent. So I did it."

In this case, the clerk acted as a team player. The clerk carried out the task of obtaining consent, did not express doubt to the intern, and in doing so, accepted the status and approval that was offered by the intern. The clerk, however, had unexpressed doubts about this situation. His/her desire to accept an offer of 'status' conflicted with an intuition that (s)he was not prepared to accept the accountability of obtaining consent.

Clerks have an obligation to perform their duties, consisting of interviews, order writing, and performing some procedures. As such, they are responsible for the suitability and consequences of their actions. The skills and knowledge of a clerk, however, are not equivalent to those of a physician. Their orders are co-signed and their actions are supposed to be checked and overseen. Thus, they are only partially accountable for their actions, for the safe-check of a superior confers a measure of accountability upon that superior. In the above case, it is unclear whether the clerk became entirely accountable for the consent, or whether the intern who should have obtained the consent remained accountable.

This case suggests other questions. Imagine that when this clerk obtained consent, they neglected to mention a small but crucial aspect of the procedure to the patient. The clerk later realised the oversight. At this point, a faithfulness to truly informed consent would require that the clerk speak to the patient regarding the omitted portion of the procedure. However, a status-oriented clerk may become more concerned with the appearance of the proper fulfilment of tasks than the task itself. Such a clerk might hold his or her tongue concerning an omission.

It is commonly said that if a history indicates that a patient was an orphan, it means that the clerk neglected to obtain a family medical history. It is easy to forget some component of a functional inquiry, and convenient to report that component as being unremarkable. In doing so, a clerk is gambling that the omission is unimportant, that their appearance of competence will be preserved, and that by not admitting to omission or error, they will continue to improve their partial status within the medical team. A clerk's sense of partial responsibility may allow him/her to believe that even if the omission is medically relevant, it will have no consequences. After all, if it is important, another member of the team is sure to catch it.

Partial status and partial accountability may also lead to ethical dilemmas related to clerks' personal ethical standards. A clerk may feel that it is inappropriate for a woman to undergo pelvic examination by more than two people at a time. Another may feel that it is insensitive for two patients of violently conflicting ethnic backgrounds to be housed in the same room. There are many such everyday ethical insights that clerks may have, but may not feel comfortable voicing because their professional status is partial. Clerks have limited influence, and yet by working in a ward they acquire a partial accountability for the events of the ward, even if these are disagreeable to their own ethical sensibilities.

Various Motivations

It is easy to say that the goal of every member of a medical team should be to provide the best care possible. In reality, a clerk has many conflicting motivations. The potential for ethical problems arising from the desire of clerks to achieve 'status' has been discussed. Another strong motivation for clerks is the desire to learn by performing procedures.²

Case 3:

"I was on call one night with an intern who was inundated with admissions. She asked me to see a patient and insert

his intravenous catheter. After two unsuccessful attempts, the increasingly irritated patient snapped, 'Do you know what you're doing?' I thought to myself: Should I try again?

The reason that clerks desire experience is that they have little. If they have little experience at performing a procedure, they will often be less competent at that procedure. If the goal of every member of a medical team is to provide the best possible treatment, then no clerk should be performing any procedures. However, clerks must practise - thus subjecting patients to their inexperienced performance - in order to acquire the ability to help a greater number of patients in the future.²

While the placement of an IV catheter is hardly a life threatening procedure, these same questions apply to other more serious maneuvers. A motivation to care may run afoul of a motivation to learn, though of course the ultimate goal of learning is to learn how to care. In specific situations, the question becomes: when should a priority be placed upon quality care, and when should learning expose a patient to inconvenience or a measure of risk?

Medical Education: Room for Change?

How can medical ethical education address some of these issues? There are no easy solutions for the questions raised. Yet, a discussion of current trends in medical education can recognize ways in which these contribute to the dilemmas discussed. Both the clinical culture of teaching hospitals, and the ethical culture of medicine contribute to the subtle but treacherous moral territory in which clerks find themselves. There are directions for change that may prove beneficial.

Recognition

Much of current ethical education focuses on 'headline' issues such as abortion, do-not-resuscitate orders, and allocation of transplant organs. These issues involve conflicting rights, and most of these debates lead to an either/or conclusion.⁵ Either the abortion is carried out, or is not. One patient gets the organ, the other does not. These issues are useful as stark demonstrations of conceptions of rights and obligations, and are important real problems. However, a medical ethical education that focuses solely only upon these issues ignores quieter and equally real ethical issues that health care professionals, particularly vulnerable individuals such as clerks, face every day.⁵ There must be a recognition of everyday ethical dilemmas as real ethical problems.

There must also be a recognition that ethical action is an entity somewhat different from ethical theory. Traditional ethical education is based upon 'basic moral principles'.⁵ While this is important, it is not enough if in practice. Non-ethical concerns lead clerks to act in violation of these principles, or they become trapped in morally ambiguous situations. It must be recognized that in addition to teaching principles, education should teach the process of ethical action in the clinic.

Cultural Concerns:

A Culture of 'Be Right', and 'Perform'

The bulk of what is tested in medical school is biomedical knowledge and skill, so this assumes paramount importance for many students. In the ongoing teaching and examination style of clerkship, many clerks feel a heavy pressure to 'be right' and 'to perform'. A lack of knowledge and skill will often result in reprimand, and sometimes in humiliation. Thus, 'being right', and 'performing' are important determinants of status. A clerk's self-doubt is a valuable part of learning, but if this is not appreciated by the team, it will go unspoken or unnoticed. This culture of 'being right' and 'performing' exists to varying degrees in different settings, but is a common experience of many clerks.⁶

While the importance of knowledge and skill is obvious, it would be valuable for clinical culture to place equal emphasis on 'asking questions' and 'being responsible'. Clerks are hesitant to ask questions concerning material or procedures that they feel they should know. The current ethos of teamwork may discourage the voicing of disagreement with a superior. More knowledgeable superiors may consciously or unconsciously 'set the standard' for what is acceptable on their wards, and it is difficult for a student to challenge these standards. In case 1, a clerk deferred to the judgement of the resident and withheld patient information. If the clerk had felt comfortable voicing an objection and had done so, the resident might have been sympathetic to the close relationship that had developed between the clerk and the patient, and arranged to have the oncologists and the clerk tell the patient immediately. In case 2, the clerk obtained consent with misgivings. Perhaps if (s)he had expressed these misgivings, the intern could have been present while the clerk obtained consent.

If clerks are only rewarded for appearing knowledgeable and competent, and reprimanded for shortcomings, there is little incentive to admit to self-doubt or mistakes. In case 2, the clerk obtained consent, not wanting to admit to doubts about his/her suitability for the task. In case 3, after trying to insert the IV catheter twice, the

clerk probably weighed the option of trying again and the option of admitting inability to the intern. In both these cases, if the clerks had felt that an admission of self-doubt or inability would not have been viewed as a failure, such an admission might have created valuable learning opportunities.

The culture of 'being right' leaves little room for personal moral qualms. In each of the cases examined, there was no clear moral 'right' or 'wrong'. These moral dilemmas rested largely upon clerks' perceptions of the situation and their relationship with patients and caregivers. While this does not make these issues any less real, the fact that they are neither clearly 'right' nor 'wrong' means they may be perceived as dissenting and bothersome opinions. They carry little weight in a culture that is heavily weighted upon 'being right' and 'performing'.

The culture of 'be right' and 'perform' values the moment. The moment that a clerk demonstrates knowledge or ability is the goal and success of training. To place more value upon 'asking questions', and 'being responsible' would be to shift emphasis towards a valuing of character as well as skill. Thus training would be concerned not only with developing a competent physician, but one who can articulate ethical concerns, who is willing to challenge superiors, and who assesses his/her own limitations of skill and knowledge.

An Ethical Culture of Decisions Instead of Process

Medical ethics' traditional focus upon 'crisis' issues and 'either/or' decisions has underplayed every day problems. In addition, this over-concern with decision as an end-point has sometimes forgotten the process of clinical ethics.³ The clinical ethical process is as complex as it is crucial for ethical action. (Note that many medical schools' ethical curricula are now becoming more process-oriented.⁴)

The clinical ethical process may begin with an intuition that something should be done differently. It may follow with a recognition of the ethical problem and principles at hand. This may be accompanied by an understanding of various parties' concerns and goals. In a complex interpersonal situation involving members of a health care team and one or more patients, the next step might be for the patient(s) and various members of the team to discuss their viewpoints in an open way. Then, a decision based on mutual understanding might be reached. All, some, or none of these steps may occur. An ethical process depends upon the skills of the individuals present, and their willingness to participate in the process. As some schools are discovering⁴, ethical teaching with

more weight on process equips students to act on their initial ethical intuition.

In the cases discussed, each of these clerks faced an inability to work through their ethical concern. Perhaps in each case, the clerk sensed the dilemma, but did not know how to address it. If their training had taught them how to constructively broach ethical concerns in a clinical context, and the kinds of solutions that could be found for these dilemmas, these clerks might not have been paralysed by their situations.

How to Change?

How can change take place? Christakis and Feudtner's research took place in 'focus group' sessions that allowed clerks to discuss ethical situations that arose in their training. In addition to legitimizing clerks' ethical problems, these sessions gave them an opportunity to talk about strategies for dealing with such situations in the future. Clerks' feedback indicated that they greatly appreciated the opportunity to discuss these concerns, and to share ideas about various coping mechanisms.²

It seems that such a group approach is effective. However, if this approach is limited to clerks, there will be limits to how much good can be achieved. The dilemmas of partial knowledge and status arise in great part from physicians' attitudes towards knowledge and teamwork. The dilemmas of conflicting motivations arise largely from a lack of dialogue between clerks and their superiors concerning everyday ethics. Thus, ongoing ethical education of physicians is a vital component in improving ethical education of clerks.

Discussion sessions wherein clerks could communicate their ethical problems to staff in a non-judgmental way would be beneficial for both parties. Such discussion would likely generate suggestions for change in the structure of a medical team. These may include a change in the way clerks are evaluated, some amendments to the hierarchy of clinical teaching, and an equal ethical voice for all on the medical team.

Evaluations could assess ability to recognize limits in one's knowledge, ability to discuss ethical objections and personal concerns, and willingness to admit error. This might create a healthier ethical climate on the wards. Clinical teaching is largely driven from the top-down. Senior clinicians have authority that derives from more knowledge and experience. While their knowledge and experience must be respected, clerks may have valuable fresh insights to contribute to a clinical setting. For the sake of learning, and the ongoing development of the hospital team, clerks should be encouraged to ask difficult questions and to challenge their superiors when they feel it is justified. If clerks are encouraged to question instructions they doubt or do not understand, they may

gain a better understanding of the rationale for procedures, or they may generate useful criticisms of routines that had gone unexamined.

Finally, the hierarchical structure within a clinical team should be made as invisible as possible when dealing with ethical questions. Ideally, there should be an understanding that anyone's ethical insights or concerns are valued independently of their rank and position. Obviously, a perfect dissociation between 'ethical' and 'biomedical' knowledge and opinion would be nearly impossible to achieve. Nonetheless, a recognition of every team member's right to a voice is the important goal.

Learning

The process of learning to be a physician is complex. Students must learn anatomy, physiology, biochemistry, pharmacology, and the list of 'ology's goes on endlessly. Clerks must also learn how to work within a team and how to navigate the waters of a hospital. Amidst all this, clerks try act as ethical and responsible individuals. Their intermediate position with respect to knowledge, status, and motivations may create quiet obstacles in their ethical lives. Learning how to work through these obstacles may, in the future, aid the clerk in case 1 to preserve trusting relationships with patients, may allow clerk 2 to voice concerns without feeling disruptive to the team, and may allow clerk 3 to know when to try a procedure, and when to ask someone to teach him/her how.

Elements that contribute to the learning environment include the clinical culture of hospitals, traditional medical ethical education, and individual teachers. At all these levels, a respect for the importance of process, and the right of each person to an ethical voice may help clerks to learn medicine and act ethically.

**Please note that it is against the policies of the University of Toronto Faculty of Medicine for a clinical clerk to obtain consent.*

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Bacterial Aortitis Secondary to *Streptococcus Pneumoniae*: A Report of a Rare but Fatal Case

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JOHN HIGGINS

Abstract

In the preantibiotic era, arterial infections were caused by endocarditis; *Streptococcal* species and *Staphylococcus* were the predominant organisms. Currently, the predominant pathogens are *Salmonella* species and *Staphylococcus*. We present a case of *pneumococcal* aortitis. A review of *pneumococcal* aortitis and aneurysms is undertaken to highlight the clinical aspects of the cases, outline the population at risk and heighten awareness to enable prompt recognition of this serious disease.

Introduction

Mycotic aneurysms were first described by Sir William Osler, in 1885 in his lectures to the Royal College of

Physicians in London. At that time the term was used to describe several aneurysms of the aortic arch from embolization of a case of bacterial endocarditis.¹ Since that time the etiology of infectious aneurysms has evolved. In the preantibiotic era the majority of these arterial infections resulted from bacterial endocarditis; consequently *Streptococcal* species and *Staphylococcus* were the predominant organisms.²⁻⁴ Currently, the predominant pathogens are *Salmonella* species and *Staphylococcus aureus*.^{2-3,5-6} *Pneumococcal* aortitis is a rare entity. In this report, we describe an unusual complication of *pneumococcal* aortitis.

Case Report

A 51-year-old male, native of Trinidad and visiting Canada for the five preceding months had been experiencing flu-like symptoms and abdominal pain for four

days. He had seen a family physician, was diagnosed with constipation and was scheduled for a barium enema. On the following day he continued to experience flu-like symptoms. After he lay down for a rest his family found him unresponsive. He was brought to the local emergency room, but was dead on arrival. He had no known prior medical problems. A post-mortem examination was performed to determine the sudden and unexplained nature of his death.

Autopsy Findings

External examination showed a well nourished man appearing his stated age with no evidence of recent injury.

The left pleural space contained 2000ml of blood (fluid and clotted), but the right pleural space was free of hemorrhage. The left lung was collapsed and atelectatic; blood was found dissecting into the parenchyma of the medial and posterior segments of the left lower lobe. The hemorrhage was originating from the posterior aspect of the thoracic aorta, just below the level of the hilum of the left lung. (Figure 1)

The aorta showed mild to moderate atherosclerosis with focal areas of severe atherosclerosis and three sites of perforation. All three sites were associated with atherosclerotic plaques. They were located within the descending aorta at three levels: just below the level of the hilum of the left lung, just above the celiac artery, and just above the aortic bifurcation. (Figure 2) The most inferior site of perforation occurred through a pseudoaneurysm 2.5 cm in diameter overlying the left psoas muscle.

Additional abnormal findings included several depressed scars and focal cortical atrophy of the left kidney.

No source of infection was noted at autopsy, and the heart valves were free of vegetations.

Microscopic examination of all three sites of perforation were similar with atherosclerosis and focal full thickness destruction of the aortic wall from abundant acute inflammatory cells. Thrombus formation with blood and fibrin deposition was associated with the lesions. The periaortic tissue had chronic inflammation and fibrosis. Gram stains showed gram-positive diplococci within the necrotic media of the aorta. The appearance was consistent with *streptococcus pneumoniae*. Sections of the hilar region of the left lung showed histological evidence of old hemorrhage with numerous hemosiderin laden macrophages within the alveoli. Other sections showed recent hemorrhage into the lung parenchyma.

Sections of the kidney showed focal interstitial scarring, interstitial chronic inflammatory cells, atrophy and thyroidization of the renal tubules - all consistent with chronic pyelonephritis.

Discussion

Although previously reported cases of aortitis and infectious aneurysms were due to bacterial endocarditis, in a review of current English literature, examining 346 patients, dating back to 1968, Johansen and Devin⁷ found that bacterial endocarditis accounts for only 17% of infectious aneurysms. Arterial trauma and depressed immunocompetence combined accounted for more than half of the cases, at 29% and 24% respectively. Arterial trauma included intravenous drug abuse, accidental trauma, surgical intervention and diagnostic procedures. Examples of depressed immunocompetence were alcoholism, diabetes mellitus, collagen vascular diseases, corticosteroid use, neoplasms, cytotoxic agents, and chronic renal failure. The remaining were classified as concurrent sepsis (17%), congenital cardiovascular defects (10%), and "primary" aortitis (3%). As a result, infectious aneurysms secondary to *Streptococcus pneumoniae* can be considered a rare entity, with only eight cases being previously reported in the English literature between 1966 to 1996.^{3-6,8-11}

Although rare, not recognising this entity can lead to a fatal outcome and therefore the clinical presentations of the documented cases will be reviewed. Of the nine cases in the literature, including the case reported above, only seven make documented clinical data available. The five men and two women varied in age from 48 to 87 years, with an average age of 62. All presented with non-specific, flu-like complaints of duration varying from days to weeks. Their symptoms included: low grade fever; atypical chest, epigastric, back, or abdominal pain; weight loss; anorexia; myalgia; weakness; diarrhea and vomiting. Risk factors for aortitis within these patients included atherosclerosis, obesity and depressed immunity (with one case each of rheumatoid arthritis and alcohol abuse). Laboratory investigations often displayed a mild leukocytosis with or without a small decline in hematocrit. Diagnosis in four cases was made based on CT images, where saccular aneurysms with reactive adjacent soft tissue changes or a slow leak were found. *Streptococcus pneumoniae* was grown from blood cultures in four cases and from aortic thrombi in two cases. Of the cases examined, three patients died: two prior to diagnosis, where a ruptured ulcerated aorta was found only upon post-mortem examination, and the third case died just prior to surgical intervention.

Overall, the clinical diagnosis of infectious aortitis with or without aneurysmal formation can be difficult. However, clinical suspicion should arise when the patient presents with a persistent low grade fever in association with any of the premorbid risk factors set forth by Johansen and Devin.⁷ Appropriate treatment with specific systemic high-dose antibiotics and surgical intervention can be initiated with early diagnosis. Since 1975 clinical out-



Figure 1: Gross photograph of the thoracic aorta perforation, with blood dissecting into the parenchyma of the left lower lobe, causing separation of the overlying visceral pleura. Probe indicated perforation.



Figure 2: Gross photograph of the opened aorta, viewed posteriorly. Three probes display the sites of perforation, located just below the left hilum, just above the celiac artery and just above the bifurcation of the aorta.

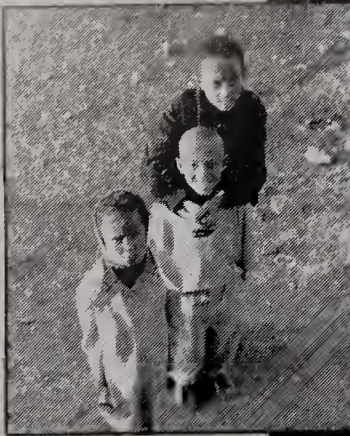
comes have improved, with 50%-100% survival rates being reported,^{3,7} with most reports emphasising early recognition as being the key to survival.^{3,5-7}

Conclusion

In conclusion, aortitis is uncommon and this report documents a rare case of *pneumococcal* aortitis. This presentation and a review of other cases is examined to highlight the clinical aspects of these patients and outline the population at risk. Hopefully, this review will heighten awareness and allow for prompt recognition of this deadly disease.

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WORLDWIDE EMERGENCY MEDICAL RELIEF

Case Records of The University of Toronto Medical School



Clinicopathological Exercises

Founded by Frank V. Ritacca, David J. Klein
and Michael S. Pollanen

Kevin O'Grady, Editor

Presentation of the Case

A 32-year old man initially presented to a peripheral hospital emergency department on Day 1 with severe, abrupt onset, right mid-abdominal pain experienced while playing golf. This pain was accompanied by nausea and vomiting. Further questioning revealed a travel history, first to the Caribbean three months ago, and more recently to Western Canada three weeks ago. The patient did not recall drinking any outdoor water nor having any other unusual experiences and was well throughout. Laboratory investigations including urinalysis were normal. An intravenous pyelogram revealed no abnormalities and an abdominal ultrasound was interpreted as normal. The patient was discharged later that same day.

The patient returned early the next morning (Day 2) in acute distress with the same abdominal pain, although he was now febrile (39°C), necessitating the use of antipyretics. Physical examination did not reveal frank

guarding or rigidity. Laparoscopy was performed and was normal except for the finding of a small amount of serous fluid in the peritoneal cavity. The appendix, terminal ileum, colon, small intestine, and gallbladder were all unremarkable. Blood tests were performed, revealing leukocytosis of $12.0 \times 10^9/L$ (normal $4.3 - 10.8 \times 10^9/L$) and an elevated AST of 181 u/L (normal 7-27 u/L). Other liver function tests and serum amylase were normal. The patient was treated with gentamicin and metronidazole.

The patient was transferred to a tertiary care hospital on Day 5. His temperature decreased to 37.5°C and his condition appeared to be improving. However, in the evening, the right mid-abdominal pain returned and his condition worsened. There was no change in his urine colour and no other urinary tract complaints. He had no chills or rigors. The next morning, he had significant nausea and vomiting. He passed some flatus, but did not have any recent bowel movements or diarrhea. Past medical history was remarkable only for recurrent right shoulder dislocations. Physical examination revealed a thin male in acute distress. There were no signs of jaundice and there were no visible skin rashes. Blood pressure was 120/80 mm Hg, heart rate was 80 BPM. The abdomen was slightly distended. Bowel sounds were present and were not increased. There was no generalized tenderness except for discomfort in the right abdomen. There was no lymphadenopathy in the neck or axillae. The lungs were clear. An abdominal CT scan with contrast was performed.

The CT scan revealed patchy areas of decreased perfusion involving the superior and mid-portion of the right kidney, which was slightly enlarged. These multiple small areas of decreased attenuation were thought to represent "renal carbuncles coalescing to form one large dominant abscess." There was no evidence of hydronephrosis, abnormal calcification, or ascites. The radiologist's opinion was "lobar nephronia or segmental pyelonephritis." Routine chemistry and complete blood

count results are illustrated in Table 1. Urinalysis results are presented in Table 2. A culture of his urine revealed no growth.

The patient was placed on intravenous cefazolin and gentamicin for several days. His pain improved each day, with his abdomen becoming soft and non-tender. On Day 9, he became hungry, and felt very well on Day 10. Antibiotics were continued until his discharge on Day 11. He was sent home with cefadroxil and was to be followed up two weeks later with an abdominal CT scan.

The patient was well until Day 15. That day, he was found unresponsive at home by paramedics. He was pronounced dead on arrival at a local hospital. A post-mortem examination was performed.

Table 1					
Serum Chemistry and Complete Blood Count Results, Day 6					
Abnormal findings are highlighted in boldface					
Variable	Day 6	Normal	Variable	Day 6	Normal
Urea	3.7	2.0-8.0 mmol/L	WBC	7.0	4.0-11.0x10 ⁹ /L
Sodium	134	135-145 mmol/L	RBC	4.25	4.50-6.50x10 ¹² /L
Potassium	3.2	3.4-5.0 mmol/L	Hb	128.0	130-180 g/L
Chloride	96	95-107 mmol/L	HCT	0.355	0.390-0.540
Albumin	38	35-50 g/L	MCV	84	78-98 L
Tot. Bilirubin	17	2-18 mol/L	MCH	30.1	27.0-31.0 pg
ALP	119	115-282 u/L	MCHC	36	32-36%
GGT	34	0-49 u/L	Platelets	233	150-400x10 ⁹ /L
AST	17	0-37 u/L			
Amylase	259	29-220 u/L			
Calcium	2.20	2.12-2.62 mmol/L			

Table 2		
Urinalysis results Day 6		
Abnormal results are highlighted in boldface.		
Variable	Day 6	Normal
Leukocytes	NEG	NEG
pH	6.0	4.5-7.5
Protein	1+	NEG
Glucose	NEG	NEG
Ketones	2+	NEG
Urobilinogen	1.7	1.7-17.0
Bilirubin	NEG	NEG
Blood	TRACE	NEG
Erythrocytes	5-10	<5
Leukocytes	10-20	<8
Casts	NONE	NONE
Epithelial Cells	NONE	<2
Bacteria	3+	NONE

Discussant’s Report

Allan S. Detsky M.D. Ph.D. F.R.C.P.(C.)
Associate Physician-in-Chief - The Toronto Hospital
Director, Division of General Internal Medicine &
Clinical Epidemiology - The Toronto Hospital

I believe the key focal finding here is the history of brief episodes of sudden abdominal pain that are intermittent and severe. What are possible causes of this symptom? Sudden crampy pain often indicates colic which is a symptom that occurs when a hollow viscus contracts against an obstruction. Colic can occur in the hepatobiliary tree, the genitourinary system, or the bowel. I am assuming that there is no bowel or hepatobiliary pathology here because of the normal visualizations, but it is possible that a gallstone was passed without being noticed. Another process that causes sudden onset of severe pain is an abscess. In this case, the abscess can be in the kidney in a manner that mostly does not communicate with the ureter so that there would be an absence of significant findings on the urinalysis (although he did have some evidence of red

blood cells and white blood cells in the urine). Another location that I have seen in the past is an abscess in the epidural space that causes referred pain to the abdomen. I have previously seen two individuals who actually underwent appendectomy for this pain when in fact, it was really coming from an epidural abscess caused by *Staphylococcus aureus*. One should also consider liver abscess and perhaps a gangrenous gallbladder as causing this kind of pain, but I am assuming from the laparoscopy, negative CT, and ultrasound that these were not present. Finally, tumour necrosis, cyst rupture, or aortic tear could cause this kind of pain. There is no evidence to suggest these problems here.

What do I make of the negative laparoscopy with "serous fluid"? To me this might indicate a possible so-called "sympathetic effusion" indicating disease in an area adjacent to the peritoneal cavity but not in the peritoneal cavity. The most obvious place here is the retroperitoneum. Once again, renal pathology might be prominent. One should also consider a dissecting aortic aneurysm as causing a sympathetic effusion together with the brief episodes of intense pain.

I now have to put together the last important focal finding, namely sudden death. There are only a few things that do this that fit with this case. One, of course, is a ruptured aneurysm. There is no mention of the patient's blood pressure and no other clues in this case of a ruptured aneurysm, but it is possible. The second is pulmonary embolism. Once again, there are no findings here to lead me in that direction other than the absence of a clear cut diagnosis (pulmonary embolism should always be considered when the diagnosis is not clear). A third possibility is cerebral hemorrhage, but there is no clue here unless it is related to the next diagnosis. Finally, there is a diagnosis that I am entertaining as most likely, namely overwhelming sepsis leading to sudden death. It is possible that all along this patient had high grade bacteremia. The "renal carbuncles" may be hematogenously spread septic emboli and all along the patient may have had endocarditis. The two complications of endocarditis that lead to sudden death are ring abscess causing complete AV block and a ruptured mycotic aneurysm. Overwhelming sepsis with septic shock or intractable heart failure from heart valve destruction, usually have a bit more of a prodrome than the story given here about the day he died. Of course it is possible that some of the history is missing.

In summary, I think the patient's most likely diagnosis

is overwhelming sepsis. Original site could be the kidney, epidural space, gallbladder, or skin (a usual port of entry for *Staphylococcus aureus*) and the patient may have had overwhelming endocarditis with complications such as a ring abscess, AV block, or mycotic aneurysm.

Clinical Diagnosis

Septicemia with complications causing sudden death.

Clinical Addendum

After submission of his original opinion, Dr. Detsky was asked to comment on the recurrent shoulder dislocations and areas of hypoperfusion in the kidneys. Dr. Detsky offered the further evaluation:

Originally I had interpreted the hypoperfusion within the kidneys as being a possible abscess as the radiologist referred to them as "renal carbuncles," which I assumed to mean pockets of pus. Once my attention was drawn to the recurrent shoulder dislocations, I immediately began to think of collagen abnormalities and the one that comes to mind is Ehlers-Danlos Syndrome. Ehlers-Danlos Type IV is associated with friable tissues throughout the body including skin, bowel wall and arteries. These people ultimately die of a ruptured viscus or a ruptured artery. When you put that together with the sudden death, then a diagnosis of a ruptured aortic aneurysm or perhaps other aneurysm related to collagen abnormality as opposed to infection (e.g., mycotic aneurysm), you can then make a unifying diagnosis.

I had to read the material given to me several times to find the section about shoulder dislocations (Dr. Detsky was not given the case report as published here but rather a series of consultants' notes and a radiology report on the patient - Ed.) but indeed it is there in the second consultant's report. This being a CPC, I then informed the Journal staff that Ehlers-Danlos Type IV would be my diagnosis but that I would have wanted more past medical history about friable tissues (e.g., skin), previous episodes of sudden pain or perhaps a ruptured viscus that occurred at some point in the past. I think it would be unlikely that Ehlers-Danlos Type IV would occur in the absence of any history except the shoulder dislocations, but never having seen this disease myself, I'm not certain. I think there probably was something wrong with this fellow's skin in the past.

One of the interesting things about this case is the way in which we recognize patterns in focal findings that

lead us to diagnoses in certain circumstances. In the setting of a CPC this diagnosis can be made by simply focussing on four findings alone: recurrent shoulder dislocations, brief episodes of abdominal pain, hypoperfused areas of the kidney on CT scan, and sudden death. I originally missed the significance of the shoulder problem but when I was told that it was important, I immediately thought of Ehlers-Danlos Syndrome even though I have never seen a case. In the real world with a real patient, I might also have ignored this key finding.

Revised Clinical Diagnosis

Complications of Ehlers-Danlos Syndrome (Type IV) with arterial aneurysm rupture

Pathological Discussion

Michael S. Pollanen Ph.D. (9T9)

At autopsy, there was evidence of recent laparoscopic surgery and a remote surgical repair of the right shoulder. The right shoulder was easily dislocated on simple manipulation.

On internal examination, the peritoneal cavity contained 2.5 L of liquid and clotted blood with large blood clots in the left upper quadrant of the abdomen. The splenic artery was the site of a 3 cm pseudo-aneurysm which had ruptured (Figure 1). Microscopic sections of the splenic artery revealed an extensive dissection of the arterial wall with the main dissection plane in the medial-adventitial border. The wall of the splenic artery revealed a granulation tissue response with active fibroplasia, and infiltration of both chronic inflammatory cells and eosinophils.

Similar arterial dissections were found in four major branches of the superior mesenteric artery, an intra-hepatic branch of the hepatic artery in the left hepatic lobe, and intra-parenchymal branches of the right renal artery. These dissections involved main arterial branches to the superior pole and middle-third of the right kidney. In these areas there were poorly demarcated wedge-shaped renal infarcts chiefly involving the renal cortex. On microscopic examination, the dissections were similar to those observed in intra-abdominal artery although many lumina contained organizing thrombi.

The portal vein was partially occluded by an organizing thrombus with a corresponding large "infarct of Zahn" in the right hepatic lobe. The subendocardial myocardium of the left ventricle showed patchy coagulation necrosis with interstitial hemorrhage.

The history of recurrent shoulder dislocation, and the presence of multiple arterial dissections in an otherwise healthy young adult is the typical constellation of clinical and pathological findings in Ehlers-Danlos syndrome (type IV).

Anatomical Diagnosis

Ehlers-Danlos Syndrome (type IV) with hemoperitoneum secondary to rupture of a dissecting aneurysm of the splenic artery, associated with multiple intra-abdominal arterial dissections, multiple renal infarcts, and right shoulder dislocation.

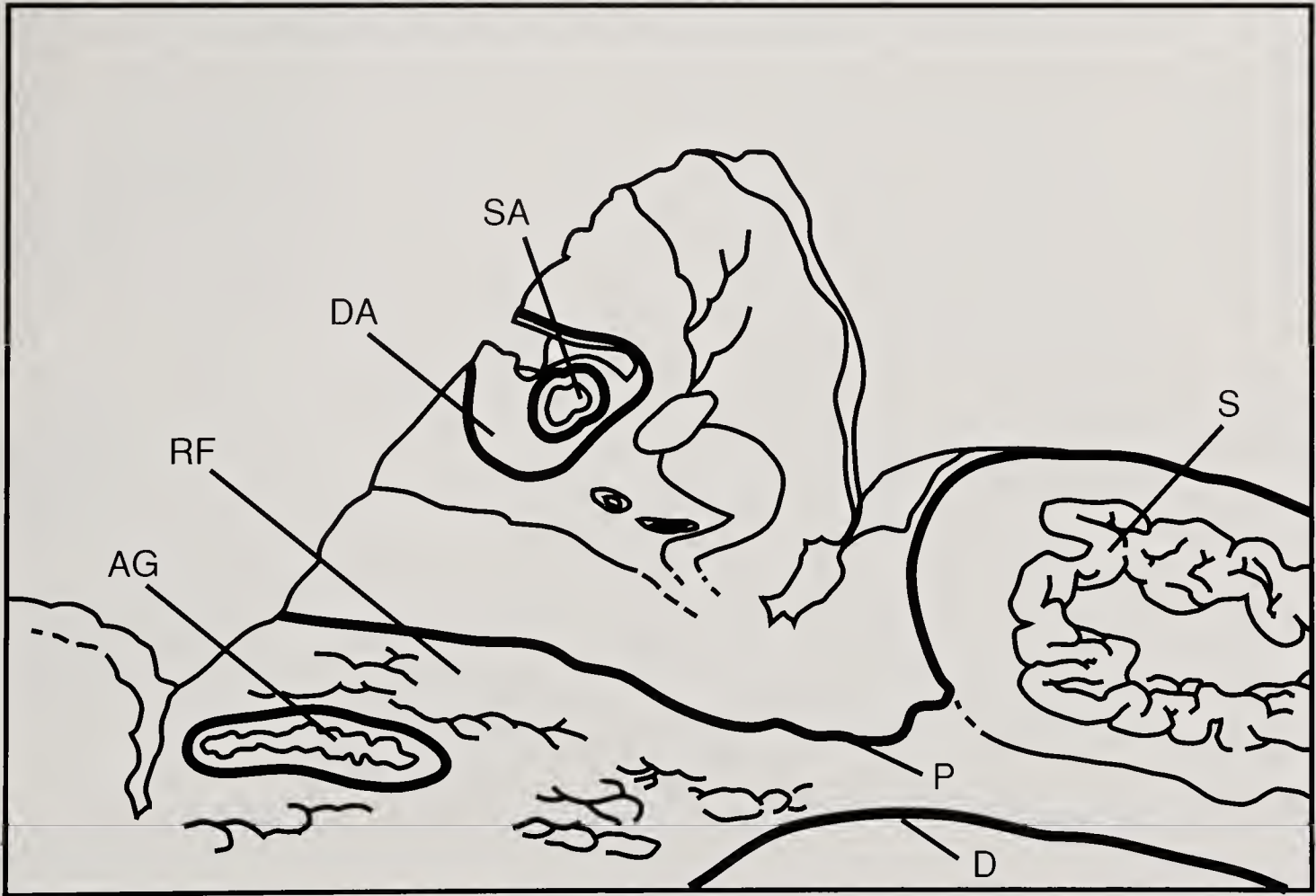
Clinicopathological Correlation

The acute onset of abdominal pain on days 1 and 2 correlates well with the multiple arterial dissections including the branches of the renal artery. The histologic features of the dissections is consistent with the interval between the initial presentation and sudden death. In addition, the decreased arterial perfusion in the right kidney observed on CT scanning of the abdomen with contrast correlated well with the renal arterial dissections and cortical infarcts. The presence of erythrocytes and leukocytes in the urine correlated well with the renal infarcts. The mildly raised AST may be explained by hepatocellular injury due to the Zahn infarct of the liver associated with venous thrombosis. Clearly, the sudden death is due to massive hypovolemia associated with the acute hemoperitoneum due to rupture of the previously dissected splenic artery. The patchy subendocardial infarction is an acute ischemic injury of the myocardium due to shock, in this case, due to massive acute hypovolemia.

Ehlers-Danlos Syndrome (EDS) refers to a group of connective tissue disorders. They are characterized by a number of genetic defects, some not yet understood. The defect in EDS Type IV is known to be due to a germline mutation in type III procollagen which is inherited in an autosomal dominant fashion. Clinical features of this disorder include thin, translucent skin with visible veins, increased bruisability, and occasionally hyperextensible joints and skin. One striking feature of EDS type IV is the propensity to sudden death from rupture of large blood vessels or viscus that are rich in type III collagen. The incidence of this syndrome is less than 1 in 5000 livebirths, with types I, II, and III accounting for the majority of cases.



Figure 1: *Sagittal section of the acutely ruptured dissecting aneurysm of the splenic artery showing regional hemorrhage in the peripancreatic fat.*



AG: Adrenal gland; RF: Retroperitoneal fat; DA: Dissecting aneurysm; SA: Splenic artery; S: Stomach; P: Peritoneum; D: Diaphragm.

KATHRYN CHORNEY

BMC Gallery

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Development of An Ovarian Follicle

1. Primordial follicle
2. Primary follicle
3. Secondary follicle
4. Maturing follicle
5. Graafian follicle
6. Ruptured follicle
7. Corpus luteum
8. Corpus albicans



By Carolyn Vermeulen "Development of An Ovarian Follicle"

Medical Consultant: Dr. Mike Wiley Medium: Watercolour & pen and ink

BIOMEDICAL GALLERY



Sympathetic
innervation
of the
pinealocyte
resulting in
melatonin
synthesis



Illustrator: Kimberley Peter

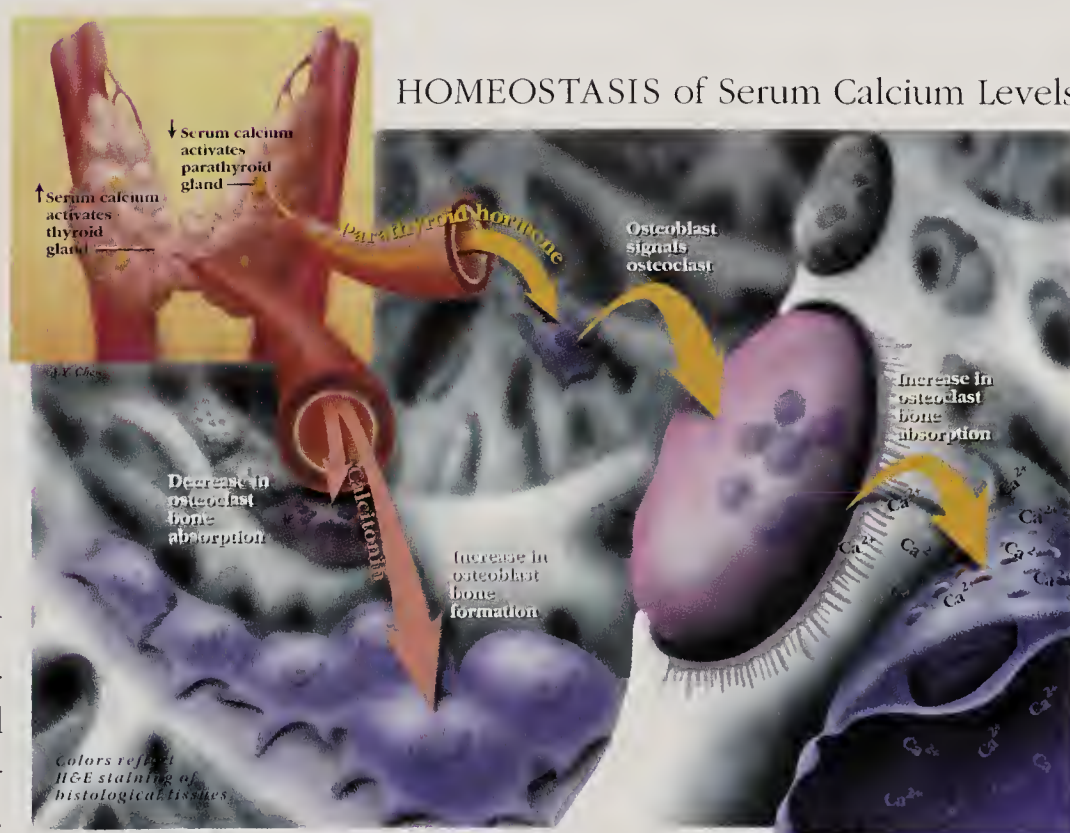
Art Consultant: Dr. Linda Wilson-Pauwels

Actual dimensions: 15x21"

Conceptual project illustrating the
sympathetic pathway and innervation
of the pinealocyte.

Medical consultant: Dr. Mike Wiley

Medical art consultant: Dr. Linda Wilson-Pauwels



By Alice Y. Chen

Histology project describing the endocrine control of osteoblastic and osteoclastic activity in bone.



The Renal Histopathology Rounds

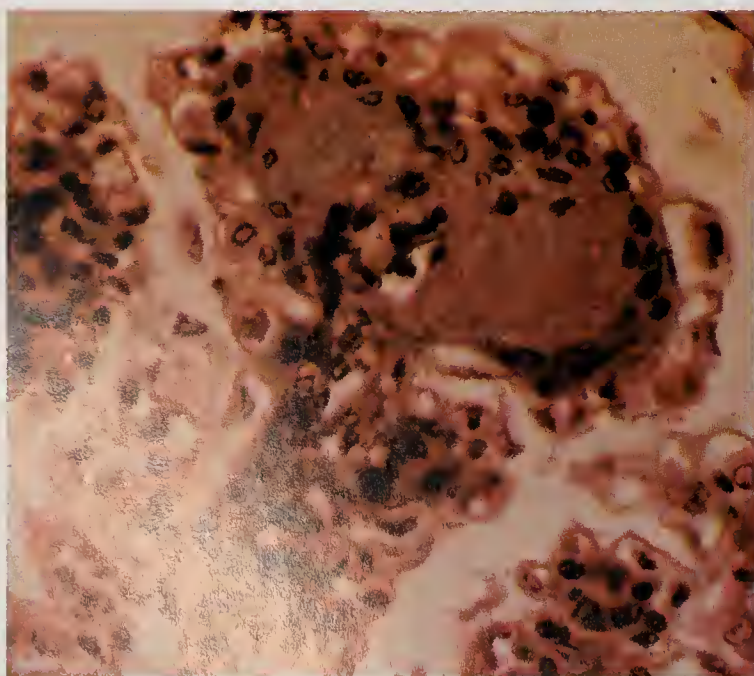
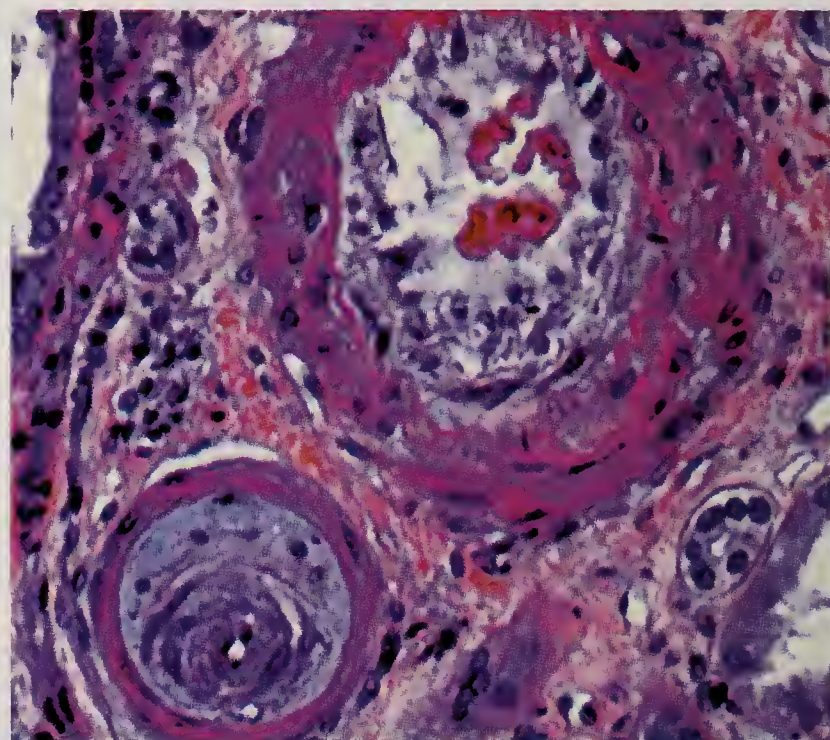
Elizabeth Hait, B.Sc. and Bonnie O'Hayon, B.A. (9T9)

The following are classic histo-pathological slides of various renal conditions. Based on the information provided, try to match each slide with the appropriate condition from the list below. (See page 48 for answers)

- 1) Membranous glomerulonephritis
- 2) Diabetic intercapillary glomerulosclerosis (Kimmelstiel-Wilson's disease)
- 3) Proliferative Glomerulonephritis
- 4) Rapidly progressive glomerulonephritis in Goodpasture's syndrome
- 5) Cytomegalic viral infection of kidney
- 6) Acute pyelonephritis
- 7) Systemic Sclerosis
- 8) Myeloma nephrosis
- 9) Oxalosis in acute ethylene glycol poisoning

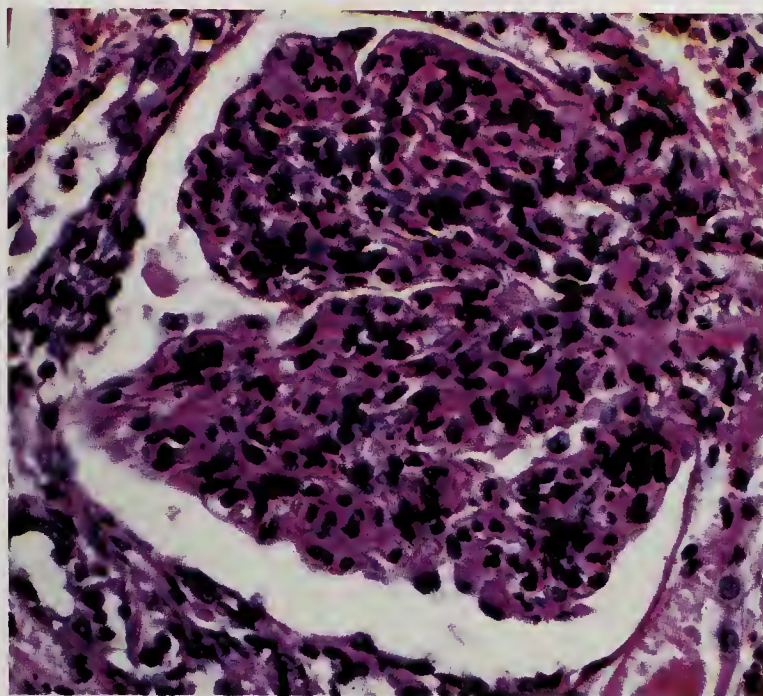
Slide A

This condition is a consequence of malignant hypertension. Intimal thickening of interlobular arteries can be seen. Collagenous material, which stains for glycoprotein is present in deposits. Intimal cells show concentric proliferation.



Slide B

The underlying disease is the major cause of renal morbidity and mortality. Deposits of hyaline material are seen in the mesangium of the lobules of the glomerulus; they are ovoid or spherical, often laminated. Hyaline may be deposited diffusely throughout the glomerulus, or in nodules; the nodules are PAS-positive, containing lipids and fibrin. Diffuse infiltration of the glomerular tuft with eosinophilic material is also observed.

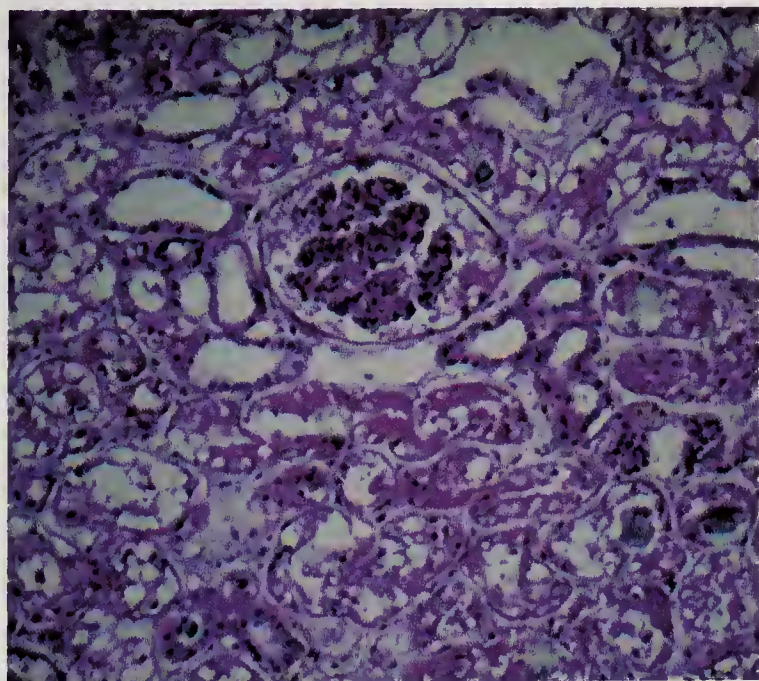
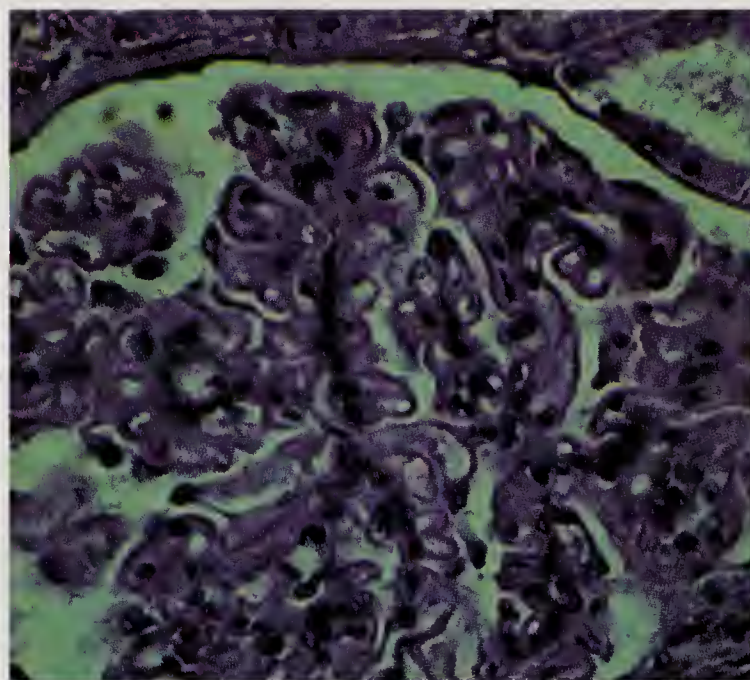


Slide C

Glomeruli are large and hypercellular. The hypercellularity is due to the proliferation of cells in the mesangium. Infiltrating leukocytes and parietal epithelial crescents can be seen. The glomeruli have a lobular appearance accentuated by proliferating mesangial cells.

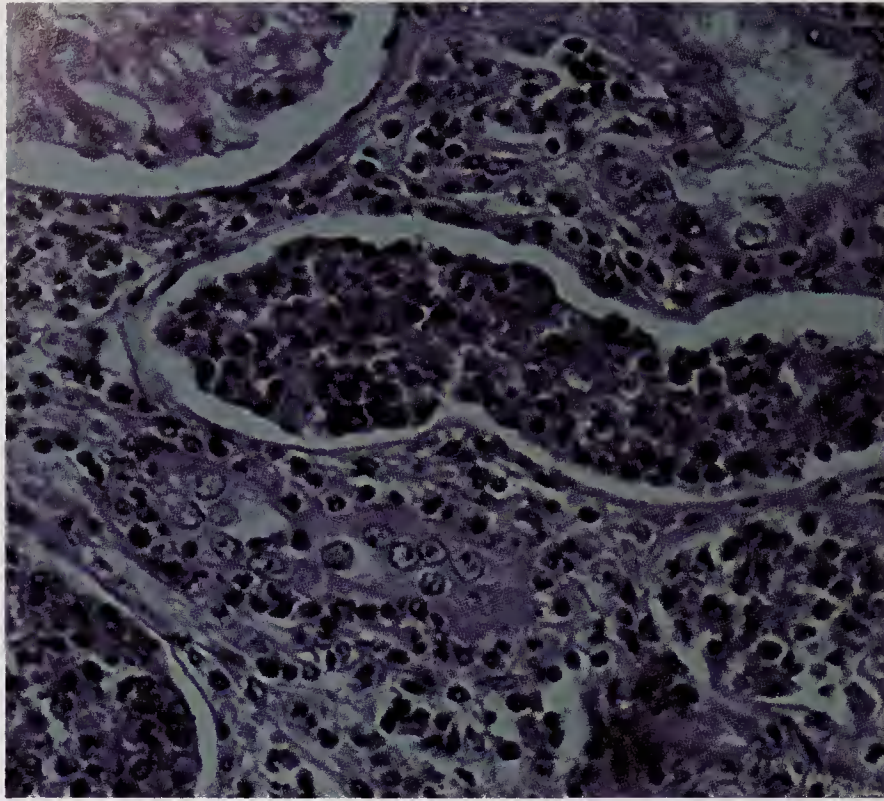
Slide D

Glomeruli range from a normal to a uniform, diffuse thickened appearance of the glomerular capillary wall. Irregular, dense deposits between the basement membrane and overlying epithelial cells can be seen. The deposits look like irregular spikes protruding from glomerular basement membrane.



Slide E

Acute tubular injury is most prominent in the proximal convoluted tubules (PCT). Renal damage from this agent causes marked ballooning and hydropic or vacuolar degeneration of PCT. calcium oxalate crystals are often found in the tubular lumina (best seen under polarized light).

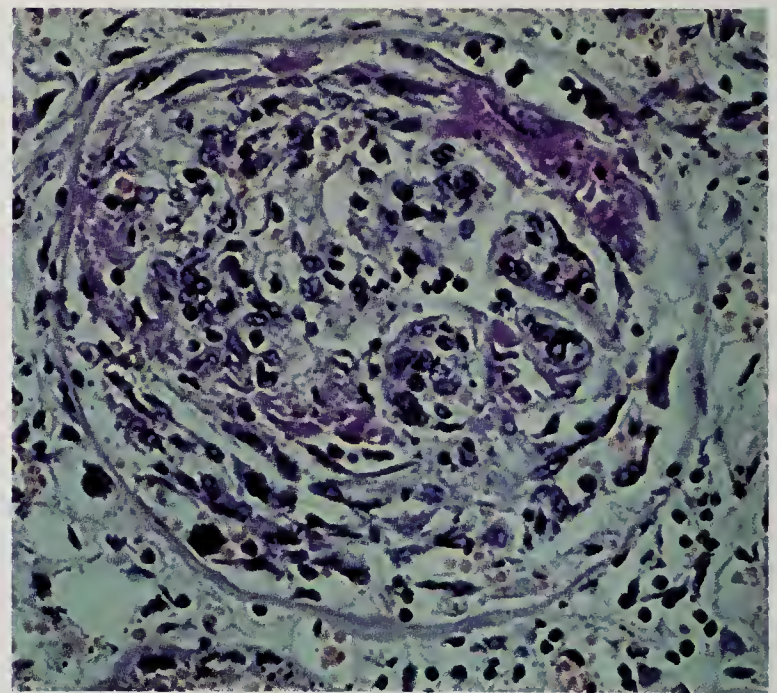


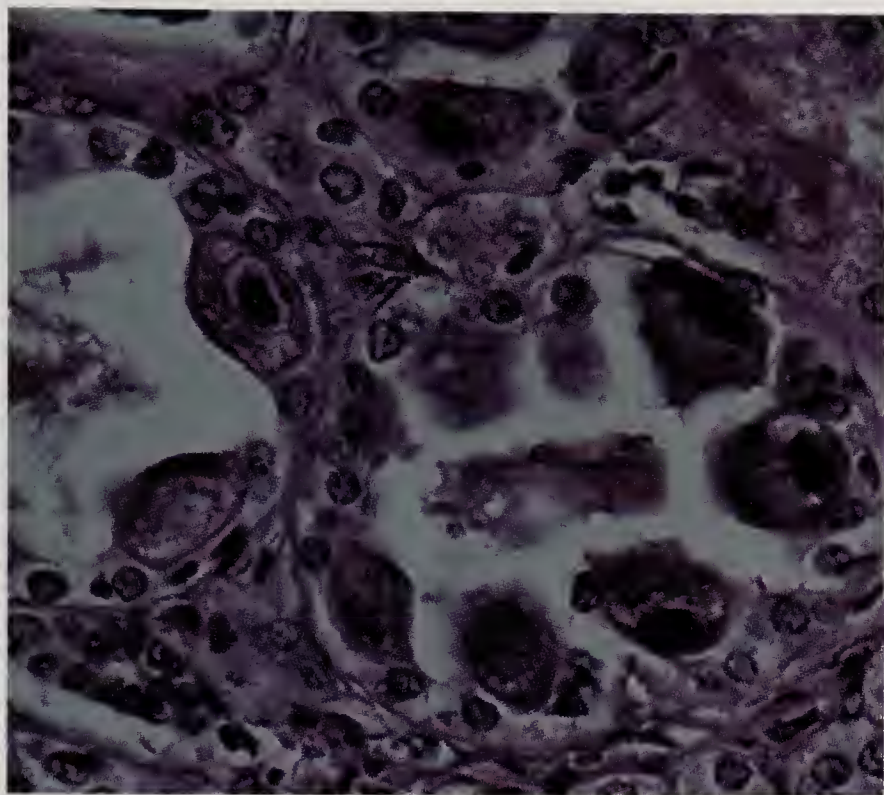
Slide F

The hallmark of this disease is a patchy, interstitial, suppurative inflammation and tubular necrosis. One can see neutrophilic infiltration of the interstitium and tubules. Large masses of neutrophils frequently extend along the involved nephron into the collecting tubules.

Slide G

In these patients there are serum antibodies that react with the basement membrane of the glomerular capillaries. The glomerulus becomes shrunken, atrophic, and surrounded by a large epithelial crescent. Many pyknotic and necrotic nuclei are present. There is eosinophilic proteinaceous material in the adjacent tubules. The tubules are lined with atrophic epithelium.



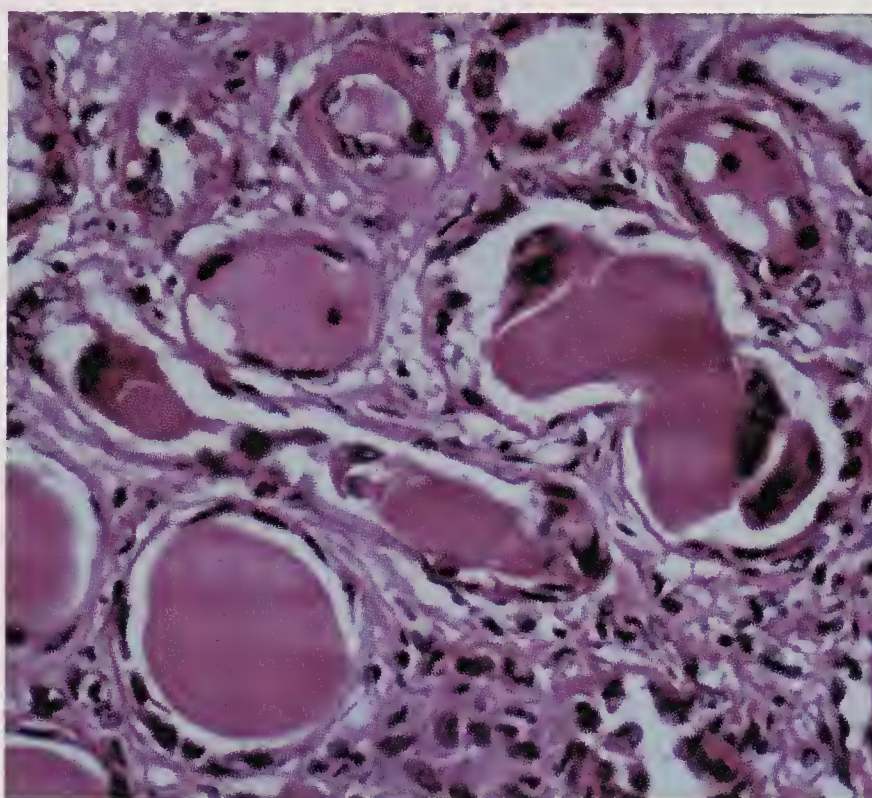


Slide H

This disease is most commonly seen in neonates or immunodeficient patients. Markedly swollen cells with large pleiomorphic nuclei with intranuclear inclusions are prominent. The inclusion may have a diameter half that of the nucleus with a clear halo surrounding it. The interstitial tissues are heavily infiltrated with lymphocytes.

Slide I

The glomeruli show PAS-positive mesangial nodules. Mild mesangial hypercellularity is demonstrated. Filling and distending the tubular lamina are Bence Jones protein casts (pink-blue amorphous masses). Some of casts are surrounded by multinucleate giant cells. The epithelium surrounding the casts are often necrotic. Adjacent interstitial tissue shows non-specific inflammatory response.



Thanks to Dr. S.N. Huang M.D. F.R.C.P.(C.), Department of Pathology, Sunnybrook Health Science Centre

Answer Key:

slide A - 7
slide B - 2
slide C - 3
slide D - 1

slide E - 9
slide F - 6

slide G - 4
slide H - 5

slide I - 8



Commercial Software in Clinical Medicine

Jordan Weinstein (9T9)

Special thanks to Dr. Peter Webster for his expert consultation.

Morning is a relative term for an ER resident on call. It simply refers to that moment when sleep ends and the day, whatever time of day, begins. At 5:00 am, the bright young intern, who was feeling neither young, nor bright, staggered into Tuktoyaktuk Memorial ER in order to begin her 48 hour shift. Weekend call was always the most interesting, and sure enough, within the hour, a spirited clerk in starched greens sought her help with an interesting admission. A 32 year old man lay motionless in curtain 4, his wife by his side was becoming increasingly anxious.

"He just started twitching in his sleep," she began in a quivering voice, "then when I tried to wake him, he started to buck and convulse. I called the ambulance immediately." Pages of Harrison's Internal Medicine began to unfold in the clerk's head; fragments of tables, graphs and incomplete reams of text danced wildly before his eyes as he haphazardly assembled a differential for seizure. His mind turned cartwheels while the droning sound of long forgotten seizure lectures emerged from the murky haze that was, at that moment, his mind. Meanwhile, the resident had started a series of Q&A with the patient's wife, piecing the episode together with great precision. The clerk stood by and awaited the inevitable, until finally, and mercilessly, that dreaded moment came.

"So, tell me," the resident began to the inexplicably terrified clerk, "what do you think is wrong with this man?" Now, at this point, in what is a typical exchange between clerk and resident, the student could resort to any of three tactics; he could swallow his pride, tuck the proverbial tail between his legs and admit that he hasn't an earthly clue; he could make a legitimate attempt to diagnose the problem, and in so doing, risk shame and embarrassment; or otherwise, in the spirit of the futuristic clerk who is on-line, in-line, e-mailed, and cruising the information Autobahn, he could do Generation X proud and simply, dutifully, ask the computer . . .

Our world, for better or worse, is becoming increasingly computerized. In fact, one would be hard-pressed to suggest a part of society which has not been helped, or in some cases rescued, by a digital hand. While industrialists and basic scientists were perhaps the originators of this modern phenomenon, everything from organized chats to organized crime has been forever changed, if not revolutionized, by the computer. As one might expect, medicine is by no means an exception to this trend. In truth, it might even be the rule.

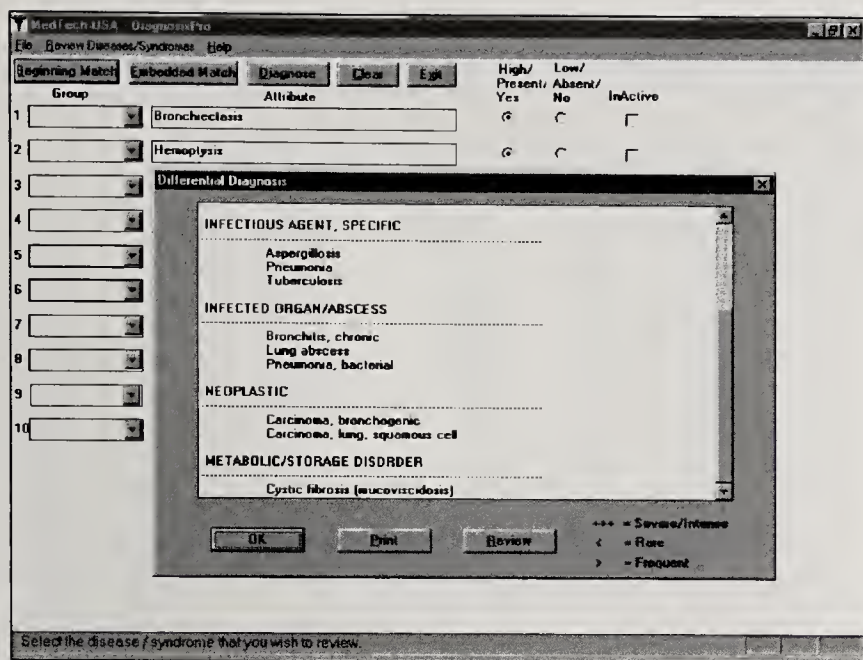
The use of computers within several medical settings has risen to startling heights. Their application in administration, research, analysis, imaging, education and communication are but a few examples. However, likely the most contentious use for medical computing, one whose merits and limitations are hotly debated, is computerization of the clinical setting. At present, many software firms are marketing their versions of "diagnostic software" with the exact intention known only to their makers. While no program is intended to replace the physician (one company says just that in its disclaimer) some programs are considered to be medical references, diagnostic aids, or adjuncts to clinical problem solving. Most current programs operate within the same basic framework: they provide a differential diagnostic hypothesis for signs, symptoms or findings entered by the user. Beyond this service, each program varies widely; some suggest treatment plans, work-ups, and even provide photographs of relevant clinical findings. In addition, a common feature of many programs is a disease reference tool, which provides an expected clinical profile for the condition of choice. The prospect that these programs might eventually become common clinical aids warrants a closer look at two such packages.

DiagnosisPro (MedTech U.S.A)

\$495 U.S.

20 MB hard disk space

DiagnosisPro is marketed as "the ultimate differential diagnosis assistant". What it may actually be, however, is little more than a categorized book of lists. The program provides an entry grid for users to indicate one or more



Screen Example #1

DiagnosisPro's differential for bronchiectasis and hemoptysis.

(up to 10) clinical or laboratory findings. One mouse-click of the "Diagnose" button found on the very simple operating bar produces a list of possible conditions which is stratified by disease category (screen example #1). In some situations, if a series of findings is significantly specific for a condition (particular threshold of this specificity is unknown) then, in the list, that entry is annotated. For example, when hemoptysis and dyspnea are entered, bronchiectasis is marked as "frequent", without any indication as to how frequent or likely.

DiagnosisPro also operates as a reference tool from another perspective. Instead of generating a differential for a given clinical scenario, the program can also list the findings one would expect for a given condition. Included in this feature is a comprehensive list of laboratory findings, and a summary of associated diseases.

Unfortunately, as a clinical problem solver, DiagnosisPro is encumbered by its crudeness and inflexibility. To begin with, when the differential diagnosis is compiled, no assessment of probability is given. Therefore, it is assumed that, with the exception of the rarely annotated entries, each possibility is equally likely on the basis of the particular scenario. As well, because DiagnosisPro considers an absolute list of findings rather than a probable one when generating a differential, incidental or confounding findings would completely stump the program. By the same token, if one was to generate a list of expected findings, there is again no assignment of odds. For example, with acute cholecystitis as an entry, one of the expected findings is clay colored stools, which would only be observed in 5% of cases (the bile duct is patent in 95% of cases of acute cholecystitis). The inclusion of laboratory findings is also quite rudimentary; only "high" and "low" is indicated as expected findings rather than a range of numerical values. Finally, the program's recognition of words is often too rigid. To help overcome

this problem, one can easily search the data base of terms (by performing what is called an "embedded match"), but overall the process is quite awkward.

To the program's credit, it is a useful "memory-jogger" and creates well categorized lists which might help students reinforce orderly thinking, especially the kind expected on oral examinations. However, DiagnosisPro is, at best, a costly and only marginally useful clinical tool.

Iliad

v4.5 (Applied Medical Informatics)

\$800 U.S.

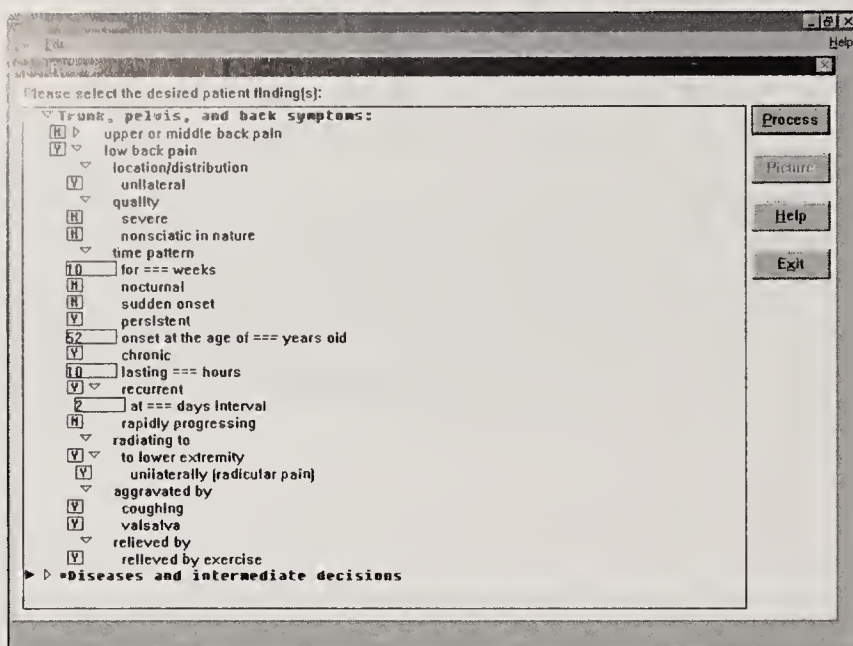
20 MB minimum - 90 MB hard disk space

SVGA

CD-ROM

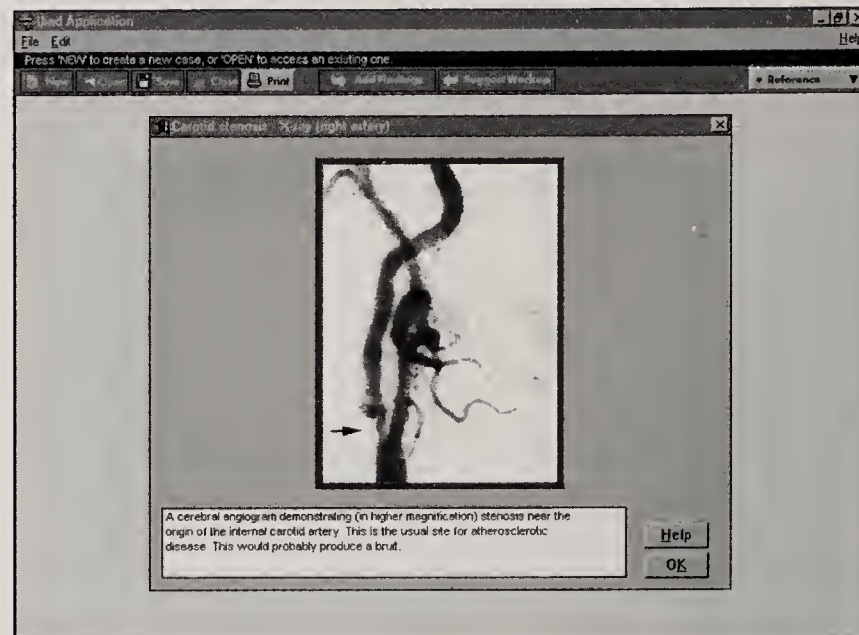
Iliad is a very comprehensive and interactive program. This package, which can occupy as much as 90 megabytes of hard drive space, is composed of three parts: consultation, simulation and reference modes. In consultation mode, Iliad allows the user to construct a patient profile based on standard identifying data (name, gender, age) and up to four chief complaints or signs/symptoms (these can be supplemented if necessary). With this information, Iliad then asks pertinent questions according a statistically driven Boolean algorithm. For example, if the chief complaint is low back pain, the user must then respond to various yes/no or numerical questions in order to characterize the pain and pertinent history (screen example #2). Iliad will then display a differential diagnosis which is stratified by disease category and ranked according to each possibility's computed likelihood. (screen example #3). The depth of Iliad's questioning becomes quite extensive for certain chief complaints, with detailed inquiries of relevant (and occasionally seemingly irrelevant) history and other clinical findings.

In simulation mode, Iliad challenges the user to diagnose a clinical problem beginning from a very brief chief complaint such as "male, age 28, presents with polydipsia". One must then piece together a history and physical/laboratory study by "asking" Iliad various questions via a simple input grid. For example, if one enters "history urination", Iliad might reply with increased "urinary frequency". Similarly, one could order a glucose tolerance test, urinalysis and a wide array of blood work if



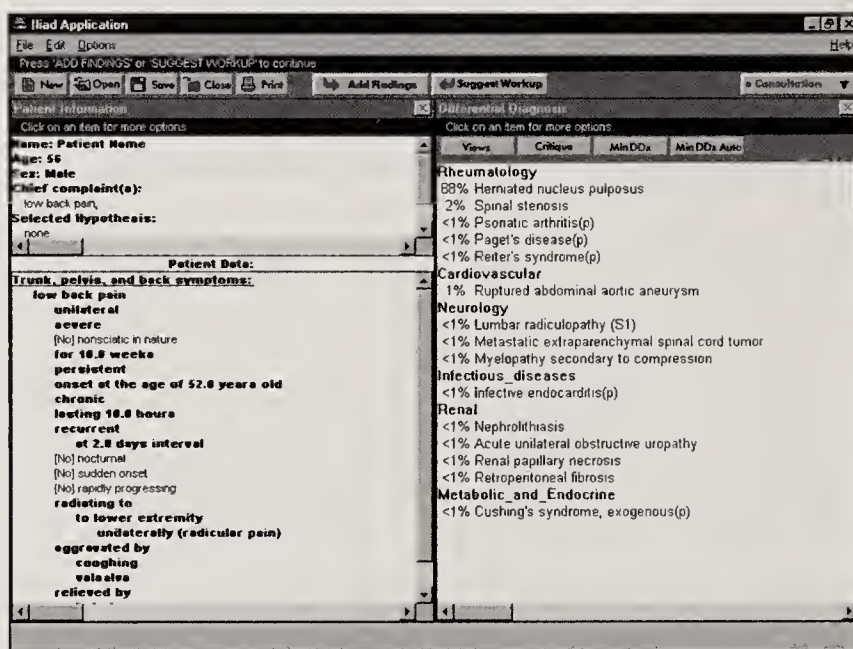
Screen Example #2

Iliad's Q&A for low back pain. A differential is then compiled, based on the answers.



Screen Example #4

An example from Iliad's photolibrary.



Screen Example #3

Iliad's differential for low back pain.

suspicious of diabetes. Thankfully, Iliad has a rather astonishing ability to recognize inputs and is not bogged down by unrecognizable entries. For example, one could obtain a urinary history by entering 'urination'; similarly, blood chemistry can be understood simply by entering 'chem'. Equally impressive is the amount of diagnostic work-up which one could order, ranging from a chest film with multiple views to more advanced procedures such as OGD or ERCP. Finally, If one becomes stymied by Iliad, then the program can provide hints and suggestions with respect to unexplored aspects of history, physical and diagnostic studies.

Iliad's exceptional reference mode has several features. Disease profiles complete with ICD-9 codes, treatment alternatives and expected laboratory and imaging find-

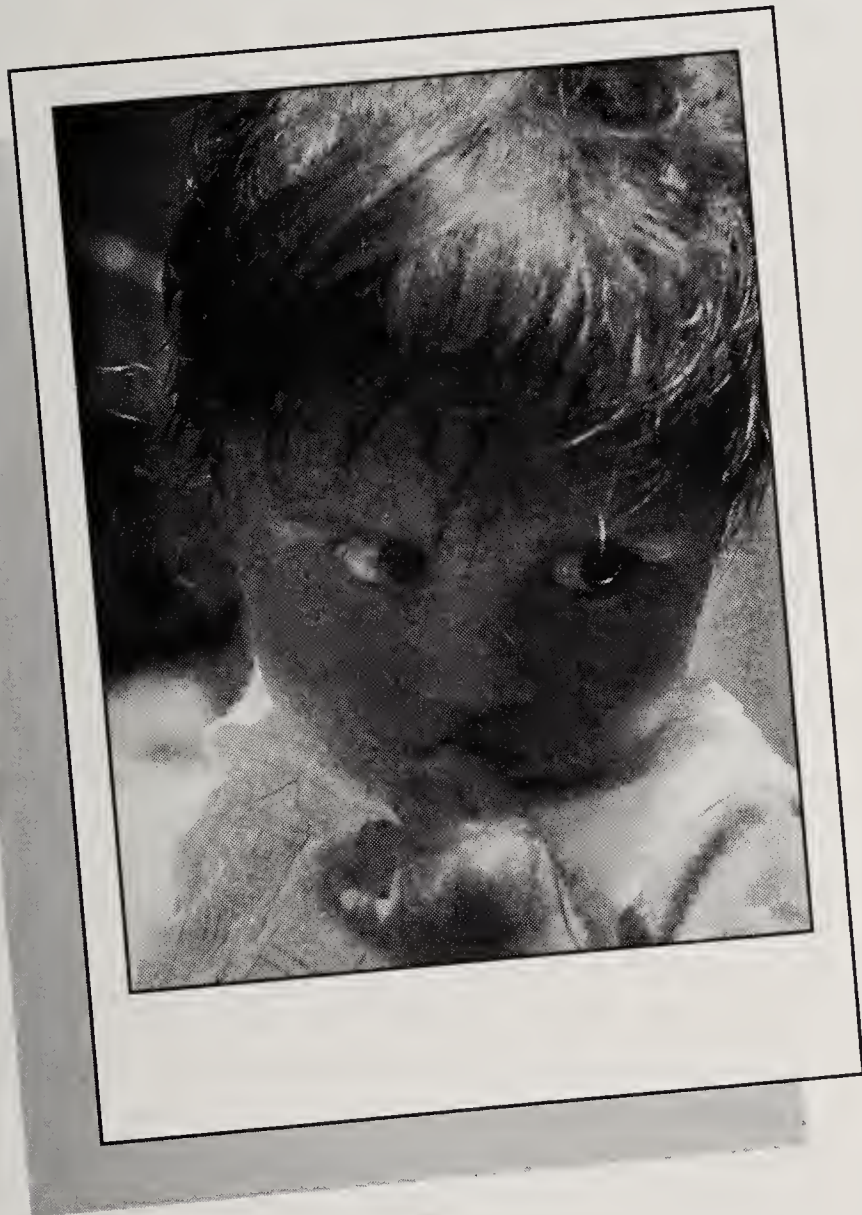
ings are available for hundreds of conditions. As well, full color photographs and radiographs are provided for a wide variety of characteristic clinical findings. A simple but rather capable search engine allows a user to quickly scan these libraries for the profile or image of choice.

The concept of Iliad is very ambitious; it is intended to be a desktop diagnostic and treatment consultant complete with a quick reference disease database. As purely a reference tool, it is a handy multimedia companion which one could use quickly and efficiently to review disease profiles and treatment options. Nevertheless, it remains to be seen whether this program would function consistently well as a diagnostic aid, particularly for complex cases. Although its language recognition is quite liberating, and even though it neatly assigns probabilities to its differential, one is still confined by inflexible disease profiles that might not account for individualized, subtle differences and confounding findings that are commonly observed in clinical practice.

The future of computers in nearly all medical fields is certainly bright. However, in terms of diagnostic problem solving, most commercial products which are presently available have mainly novelty value, at considerable financial cost, and only limited diagnostic usefulness. Nevertheless, these programs might be of benefit for students who are learning basic clinical reasoning and for systematic, efficient review of disease profiles by category. And so until proven otherwise, the best approach to clinical problem solving remains in the human realm, while computers continue as our dutiful and inferior subordinates who toil diligently behind the scenes — much like clerks.

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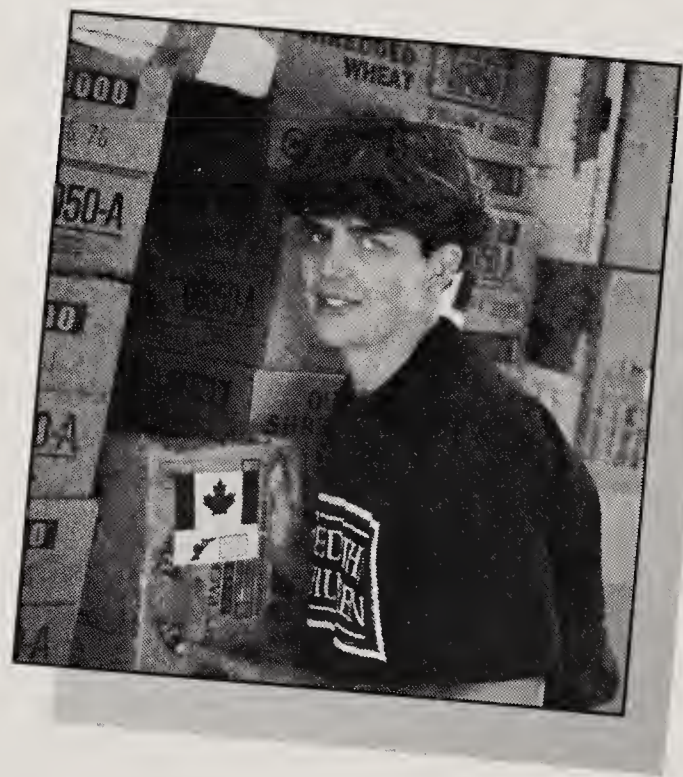
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Practical Diabetes Care

Rowan Hillson

Oxford University Press, 1996

\$57.50

In this book, Dr. Hillson sets out to provide health care professionals with a practical manual on the management of diabetes mellitus that can also be used as a quick reference. Transatlantic differences aside, she achieves her goal.

Practical Diabetes Care includes detailed, pragmatic information on diagnosis, monitoring, nutrition, exercise, treatment, and complications in diabetes mellitus. The author has also included chapters that deal with work, travel, cross-cultural, and developmental issues for the diabetic patient. The general practitioner who wants to set up a diabetic clinic will find a chapter that briefly examines the process from planning through to evaluation with many suggestions for equipment and staff.

The information is up to date and presented in a readable manner. The author has integrated the underlying pathophysiological mechanisms and psychosocial concepts into her discussion of each area. Dr. Hillson presents and critiques different approaches to monitoring and treatment and emphasizes the importance of educating the patient to achieve optimum diabetes control.

Dr. Hillson's writing style employs short, concise sentences and she has used a problem-solving approach that includes short case scenarios to illustrate her points. The body of the text is subtitled and supported throughout by well labeled illustrations and tables, making it easy to read. Each chapter ends with a bulleted summary that emphasizes the main points.

Some of the pharmacological information and all of the information on social support resources reflect the fact that this book was written in the UK making these chapters less useful for the Canadian health care professional. This is a small percentage of the information contained in the book. When one balances the many strengths of this book (clear, informative and multidimensional) against the minor weakness of its UK perspective of

social supports, it becomes clear that *Practical Diabetes Care* is a worthwhile resource for family doctors, medical students and health care professionals.

Barbara Crawford, B.Sc.N. (9T9)

Epilepsy: The Facts. (2nd Ed.)

Anthony Hopkins and Richard Appleton

Oxford University Press, 1996

\$22.95

Epilepsy is a disease that has been shrouded in mystery for centuries, and is even referred to in the Bible. It is a disorder characterized by recurrent and abnormal discharges of brain cells manifesting into various medical syndromes. Appleton and Hopkins wrote *Epilepsy: The Facts* in order to destigmatize and dispel the myths of epilepsy by informing the general public and physicians about this common condition. The authors, achieve their goals in a clear, concise summary of the subject.

The contents of the book include a basic definition of epilepsy, a description of the various types of seizures, as well as a factual chapter describing the causes of the disease. It contains many useful tables and charts which aid in making mountains of information manageable. References to recent studies and data are found throughout the text, however, precise sources from journals are unfortunately lacking; with neither footnotes nor endnotes. As a result, the more advanced reader cannot easily delve deeper when the interest is there. Also included in the text is a list of international organizations for those with epilepsy.

The authors do provide an excellent summary of the current treatment of the various forms of epilepsy, including useful tables describing drug doses, adverse effects, as well as a description of when to use which drug. The authors also consider the importance of surgery as a treatment modality, acknowledging the pioneering work by Canadian neurosurgeons Penfield and Rasmussen. The treatment of status epilepticus (every intern's nightmare) briefly discussed.

"Living with Epilepsy" titles one chapter, and is excellent at providing the physician with a perspective on epilepsy that most textbooks lack, – the patient's. However, due to the fact that the book is written by British professors, discussions of employment, driving and insurance are anglo-centric and not very useful to the Canadian reader. Nonetheless, the chapter provides a different view of an important aspect of the disease. Following that is a somewhat misplaced chapter describing the common problem of febrile convulsions. The body of text concludes with a brief probe of current research, and a plea for more research money.

Overall, this book does provide a good introduction to epilepsy for those with some medical knowledge. The weakness of the book is that it seems to be aimed neither at the doctor, as at times it lacks depth and isn't referenced, nor at the patient or worried parent who may find the text too "medical". As for the medical student, this book can provide him or her with a useful starting structure on which to build a more complete understanding of this intriguing disease.

Mary Hassard, B.Sc. (9T9)

Essential Anaesthesia for Medical Students

Mark Heining, David Bogod, and Alan Aitkenhead

Oxford University Press, New York, 1996

\$35.95

Essential Anaesthesia for Medical Students is one of the better-organized books that attempt to review a field of

medicine concisely; yet it accomplishes its purpose without appearing superficial. It is written by anaesthetists at Nottingham University Medical School whose teaching approach is governed by the "new curriculum." This book enforces the existing knowledge of medical students by applying principles learned in "integrated courses" to the field of anaesthesia.

The book is divided into two sections (each of five chapters) that review the role of the anaesthetist inside and outside the operating room. Details of practical procedures have been deliberately omitted from the book for sake of brevity. These skills can be learned more efficiently through 'hands-on' experience rather than by perusing through pages of small text. Instead, this book provides the foundation for learning those skills and provides medical students with the confidence to tackle their anaesthesia rotation. The first section begins by explaining how anaesthetics work, the hazards associated with their use, and current controversies in the field. Subsequent chapters describe the different methods of introducing anaesthesia, and the different drugs that are used. The first section ends by explaining the principles behind the monitoring and functioning of anaesthetic equipment. The book is written clearly and is easy to understand. Also, it is not without a sense of humour. For example, the signs of unexpected bleeding in a patient on the operating table are described as "shouting, muttering, or total silence", but the cardinal sign is "absence of chatter about golf or the stock market" by the surgeon.

The strength of this book lies in its use of tables to present crucial facts; for example in comparing the advantages and disadvantages of general versus regional anaesthesia, or the route of administration for anaesthetic drugs. After reading this book, twenty minutes spent studying the tables would be sufficient for the average medical student to retain the key messages. To aid retention, each chapter ends with a section that is conveniently labelled "Key Points", which summarizes ten pages of an easy-reading book into ten lines of pointers.

Since the role of the anaesthetist is not limited to the operating room, the second section covers peri-operative assessment, pain management, and intensive care. Recognizing that things can go wrong for even the most accomplished anaesthetist, the book ends with a review of CPR. Since the knowledge of just the 'basics' of anaesthesia (typical of medical students) can be dangerous, the second section explains how to modify the principles learned in the first section to deal with complex situations; for example, dealing with diabetic patients

who suffer convulsions post-operatively. A complete index and table of contents allow quick access to this type of information. Since the book is not a thorough reference-text, the authors suggest 2-3 valuable books that the medical student can refer to for more information at the end of each chapter.

Despite its aforementioned strengths, there are two areas in which this book falls short. While the text is appropriately clear, some figures are confusing due to oversimplification. Adequately labelled figures could have complemented the excellent tables. Secondly, at \$35.95 this 150-page book is overpriced by \$15. A medical student investing another \$40 could purchase a comprehensive textbook. However, for the student wishing to learn as much as possible about anaesthesia within three hours, *Essential Anaesthesia for Medical Students* is an excellent choice.

Ali Islam, B.Sc. (9T9)

Everyone's Guide to Outpatient Surgery

James Macho and Greg Cable

Someville Publishing House, Toronto

\$ 19.95

Fiscal realities in the last 10 years have changed the way medicine is practised in North America. Not only are physicians expected to provide good medical care but they are required to do it cost-effectively. The economic influences on the delivery of care have led to the ever increasing popularity of day-surgery.

In day-surgery, the patients come in for surgery in the morning, they are operated on during the day and they are discharged usually after 2 hours of stay in the recovery room. This saves hospital beds and reduces the cost of the operation considerably. Obviously, this can not be done for every operation but the tendency is to do most surgery in this setting. There are, however, some disad-

vantages to this process. In day-surgery, the patients get less pre- and post-operative contact with the surgeon than in an inpatient setting. This may lead to anxiety in the patient's mind about the quality of care that he or she is receiving compared to that being provided to the inpatient. Moreover, there are fewer chances for the surgeon and the patient to discuss the procedure and this could be a source of added concern.

Everyone's Guide to Outpatient Surgery is written with these points in mind. It is a source of information designed specifically for the patient. In simple every day language, this book addresses several important issues faced by a patient who has been told that he needs surgery. The book takes the patient through different stages of decision making and planning for day-surgery. It tells the patient what questions to ask his/her surgeon about the need for surgery, the risks involved, and the procedure itself. There is also a description of the admission process and tips on dressing and travel arrangements so that the process is as easy for the patient as possible. There is even a section on paediatric day-surgery for parents of children undergoing surgery.

Anesthesia is a big concern for a number of patients. *Everyone's Guide to Outpatient Surgery* devotes a whole chapter to this topic. In jargon-free language, it describes the different kinds of anesthesia that are available, the different pieces of equipment used by anesthetists, and the advantages and disadvantages of the different types. The book then details the experience of anesthesia, from the patient's point of view, from the time when the anesthetist first meets the patient to when the patient "wakes up" in the recovery room. It reassures the patient by depicting the very active role the anesthetist plays in the care of the patient, both in the operating room and in recovery. Again, a section is included on anesthesia for children.

The most interesting part of *Everyone's Guide to Outpatient Surgery* is its information section which is a database of different surgical procedures. Most of the book is devoted to this database. Each chapter includes procedures that are performed in day-surgery by a different specialty. The chapter, simply and briefly describes the relevant anatomy, physiology, and pathology with illustrations that explain the concepts well. There is usually a description of the common procedures that are performed to diagnose or correct surgical problems. Where appropriate, a discussion of laproscopic versus open procedures is also included. It then goes on to describe the steps to recovery from the operation. Each chapter also includes a very useful list of specific ques-

tions that the patient can ask the surgeon about surgeries in that particular specialty. All in all, this section is quite well done.

Everyone's Guide to Outpatient Surgery is a simple to understand, yet very informative book. Although it could be used by clinicians as a general reference, it lacks the technical detail that would be required by clinical practitioners. In fact, the absence of strict clinical terminology is a big strength of the book that makes it accessible to individuals without the benefit of medical training. It is primarily meant for patients and they are the ones who will benefit from it the most. If one is looking for a book to recommend to patients to learn more about their suggested surgery, then the breadth of coverage, simple narration and easily understood language of *Everyone's Guide to Outpatient Surgery* make it a very commendable choice.

Khalid Syed B.Sc. (9T9)

Medical Parasitology - A Practical Approach

S.H. Gillespie and P.M. Hawkey

IRL Press (Oxford University Press), New York 1995

\$89.50

The focus of this book – one in a line of *Practical Approach* manuals – is to identify and explain the main laboratory diagnostic approaches to the principal parasite infections found in patients not resident in endemic areas (i.e. travelers to areas of endemicity returning with signs and symptoms of parasitic infection). The book, the first edition, aims to bring the protocols used to diagnose tropical and some temperate parasites into the mainstream of clinical microbiology.

Each chapter (except for the first which serves as a general introduction) is authored by a specialist in a particular parasite species. The backbone of each chapter is the assessment of the key laboratory diagnostic tools

available in the identification of the parasite. This is accomplished by essentially listing the various protocols – be it simple light microscopy with staining, culture of the organism from specimen, or more recent molecular approaches including enzyme-linked immunosorbent assay (ELISA) – used in the parasitology lab. At the beginning there are a collection of not very comprehensive visual “plates” or photographs of what one would expect to see under light microscopy for various parasites. It should be noted though that atlases of parasitology cover in much greater depth and breadth the multiple forms in which one might see parasites.

Each chapter begins with a brief introduction into the particular organism and the extent of the disease epidemiology. Some chapters are authored by individuals who place greater emphasis on symptoms and clinical setting for the disease. For example, the malaria chapter describes clearly and concisely the “clinical features” and “pitfalls in diagnosis” associated with malaria and then indicates the importance of the travel history. Other chapters pay less attention to the clinical setting and delve straight into the diagnostic strategy based on laboratory evidence. Many chapters indicate the importance of the life cycle of the organism in question and how this may confound attempts to correctly diagnose strategies, details of the particular protocols used in the laboratory, and less on the clinical presentation and epidemiology of the disease. While the book is subtitled as “a practical approach”, it might be more accurate to indicate at the outset that this is largely a manual in laboratory techniques.

In general, the writing is lucid and precise with liberal use of tables and figures as explanatory tools. Once again, the fact that much of the text is attributed to laboratory protocols interrupts the flow, giving the feel of a manual rather than a text per se. The book assumes prior laboratory experience and facility in techniques in clinical microbiology, especially the use of stains and ELISA approach strategies outlined. There is much evidence now that PCR-based diagnosis and speciation (for example, distinguishing *P. falciparum* from *P. vivax*) is a well-established tool in molecular diagnosis. The various authors may have done well to outline in greater detail the PCR-based strategies to a variety of parasites, not simply malaria. The book is intended for the clinical laboratory as another methods manual – but this time for the more esoteric tropical bugs that are now entering the mainstream of discussion due largely to increased travel.

The final note should be on the cost (C\$89.50) which may be excessive considering the book is only paperback and relatively short at 295 pages with few colour plates.

Dylan Pillai, B.Sc. (MD/PhD program, year 3)

Vascular Diagnosis, 4th edition

Eugene F. Bernstein

Mosby, St. Louis, Missouri 1993

Vascular Diagnosis is a medical reference text which provides information on the current state of laboratory technology used in the clinical investigation of vascular disease. The editor-defined goal of *Vascular Diagnosis* is “to provide guidance to the physician planning to initiate and direct a vascular laboratory, the practitioner with a clinical problem to analyze, and the researcher who needed to know the state of the art to improve upon it.” The scope of this goal is quite broad, and the intended audience – laboratory directors, practitioners and researchers – is very diverse. Therefore, it is not surprising that *Vascular Diagnosis* falls short of achieving its goal. While vascular laboratory directors and individuals researching vascular diagnostic technologies will find that *Vascular Diagnosis* is a good and complete reference, practitioners will find that it does not entirely address their clinical needs.

Vascular Diagnosis is the most recent edition in the *Noninvasive Diagnostic Techniques in Vascular Disease* series. The title change reflects the inclusion of “semiinvasive” techniques such as transvaginal ultrasound visualization of the pelvic vessels and endovascular ultrasound probes for atherosclerotic plaque visualization. *Vascular Diagnosis* is divided into four parts: I. General Aspects of *Vascular Diagnosis*; II. Fundamentals of Measurement and Current Instrumentation; III. Areas of Application: Detection, Quantitation, and Prediction; and IV. New Applications and Directions in *Vascular Diagnosis*.

An excellent, albeit brief, description of patient history and physical examination in vascular disease is provided in Part I, which deals with primarily establishing, accrediting, and running a competent vascular laboratory. The basic science underlying blood velocity measurement (using Doppler and real-time ultrasound imaging), pressure measurement (using direct and indirect methods as well as ocular pneumoplethysmography), volume measurement (including impedance, mercury strain-gauge and air plethysmography), and vascular imaging is discussed in Part II.

Information regarding the practical applications of diagnostic technologies to specific vascular diseases is presented in Part III, which is the most extensive section of *Vascular Diagnosis*. Various methods that may be used to investigate extracranial occlusive disease, peripheral arterial disease, abdominal vascular disease, and peripheral venous disease are examined in detail in this section. Most of the chapters in Part III provide a discussion of the use of a particular diagnostic technique to evaluate a particular vascular disease. Occasionally, a diagnostic protocol is proposed which details the most cost-effective method to investigate a specific condition. The excellent chapter on the comparative value of laboratory tests for the diagnosis of venous thrombosis provides such an analysis. Although some experimental techniques are discussed in Part III, most of the future directions for vascular diagnosis are presented in Part IV, which includes chapters on intravascular ultrasound, ultrasound contrast agents, and magnetic resonance angiography.

Unfortunately, *Vascular Diagnosis* provides very little guidance for the clinician who must ultimately make the decision as to which laboratory investigation, if any, is appropriate based on patient presentation, history and physical examination. However, clinical highlights may be found in the chapters on the spectrum of ischemic cerebrovascular disease and problems in peripheral arterial disease.

The 124 chapters of *Vascular Diagnosis* were written by a total of 114 authors, providing expertise in each of the fields addressed. Each chapter is discrete and comprehensive, but there is little continuity or flow between chapters. In addition, there is a significant amount of repetition amongst chapters. For example, the Doppler equation is defined and described in eight different chapters. In certain instances, there are two chapters on the same topic, such as the applications of intravascular ultrasound. Although much of the information may be repetitious, the differing perspectives of the distinct authors may be enlightening to some readers.

The diagrams in *Vascular Diagnosis* are generally of very

good quality, particularly the reproductions of color Doppler images. In addition, the index is comprehensive and well organized. Most individual chapters are written clearly, however, the transition between chapters is abrupt and critical summaries of the diagnostic techniques for individual vascular diseases are noticeably absent. Some previous knowledge of vascular diagnostic technologies and/or the theory underlying their function is assumed throughout. As a result, *Vascular Diagnosis* is most appropriate for those familiar with these investigative technologies.

The focus of *Vascular Diagnosis* is clearly to detail and describe the technologies used in vascular disease diagnosis, and not to guide the clinical practitioner from initial patient presentation to diagnosis of vascular disease. Consequently, the book would be more appropriately titled *Diagnostic Techniques in Vascular Disease*.

In conclusion, *Vascular Diagnosis* would make a valuable resource text for specialized medical practitioners who work closely with a vascular laboratory and diagnostic scientists working to advance the technologies used to diagnose vascular disease.

Peter Ballyk, M.Sc. (MD/PhD program, year 5)

Dictionary of Endocrinology and Related Biomedical Sciences

Constance R. Martin

Oxford University Press, Canada 1995

\$107.50

The *Dictionary of Endocrinology and Related Biomedical Sciences* is a well organized and clearly illustrated endocrinology reference text. It provides a comprehensive description of terms used both by endocrinologists and those in related biomedical sciences, in a form that is readily comprehended by readers previously unfamiliar with them. Its usefulness as a reference tool is also enhanced as it indexes commonly cited acronyms and chemical trade names.

Its scope encompasses not only the vast cornucopia of hormones, neurotransmitters, vitamins, enzymes, and other regulators, but also includes the structures, biosynthesis and metabolism of those regulators, the receptors activated, second messengers generated, and the biochemical pathways involved. The clinician will find useful descriptions of the causes and manifestations of endocrine system dysfunctions, as well as methods of treatments and the therapeutic agents employed in their treatment. Scientific investigators will also find this dictionary helpful as it includes the pharmacological agents unsuitable for use in humans that mimic the actions of naturally occurring cell components or disrupt their functions. It also includes references to statistical and other procedures for analyzing data. While there is some emphasis on human physiology and dysfunction, this work also contains numerous observations made on lower organisms as well as many obtained from *in vitro* systems.

The amount of detail with which each term is described is reasonably sufficient as the publication averages about 12-13 entries per page, where by comparison an English language dictionary of comparable size averages between 28 and 29 entries per page. Furthermore, the information in this text is presented to the reader in a form that ties together both the endocrinological and the physiological significance of the defined terms. The result is a text that goes somewhat beyond that of a simple dictionary.

Where appropriate, clear diagrams of the chemical structures are provided alongside the IUPAC chemical compound names for ease of comparison between similar structures. In addition, the secondary structures of polypeptide hormones are included as well as their pre-pro forms.

The text is well written in a concise form that is neither confusing nor bogs the reader down with complex detail obtainable from specialized texts. The level of previous knowledge in the field required to make use of this text is such that it could be of value to any person with a basic level of understanding of physiology and/or endocrinology. Therefore, it is not only of use to the practising clinician or established investigator, but also to the future health care professional or researcher.

In my opinion the *Dictionary of Endocrinology and Related Biomedical Sciences* is an excellent, comprehensive reference text for those pursuing the field of endocrinology or many of its many affiliated sciences. As a medical student, I found it to be quite useful and would recommend its addition to faculty and student resource libraries. However, with a price of \$107.50 it would seem hard to justify its purchase by the undifferentiated medical practitioner or general physiologist.

Mark T. Nutley, M.Sc. (9T9)



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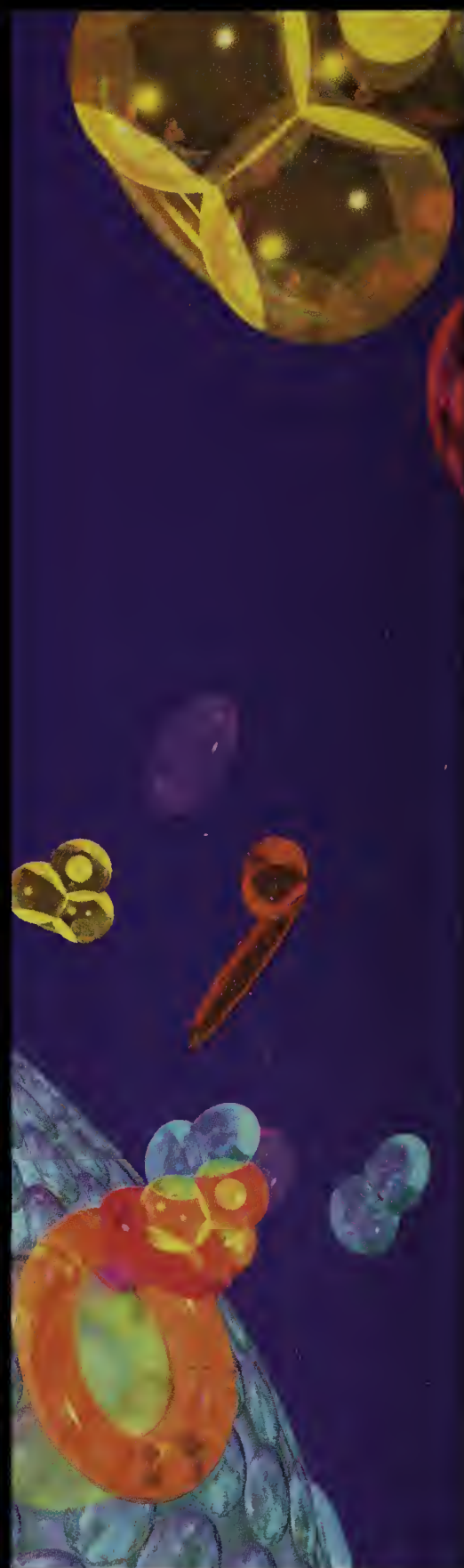
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